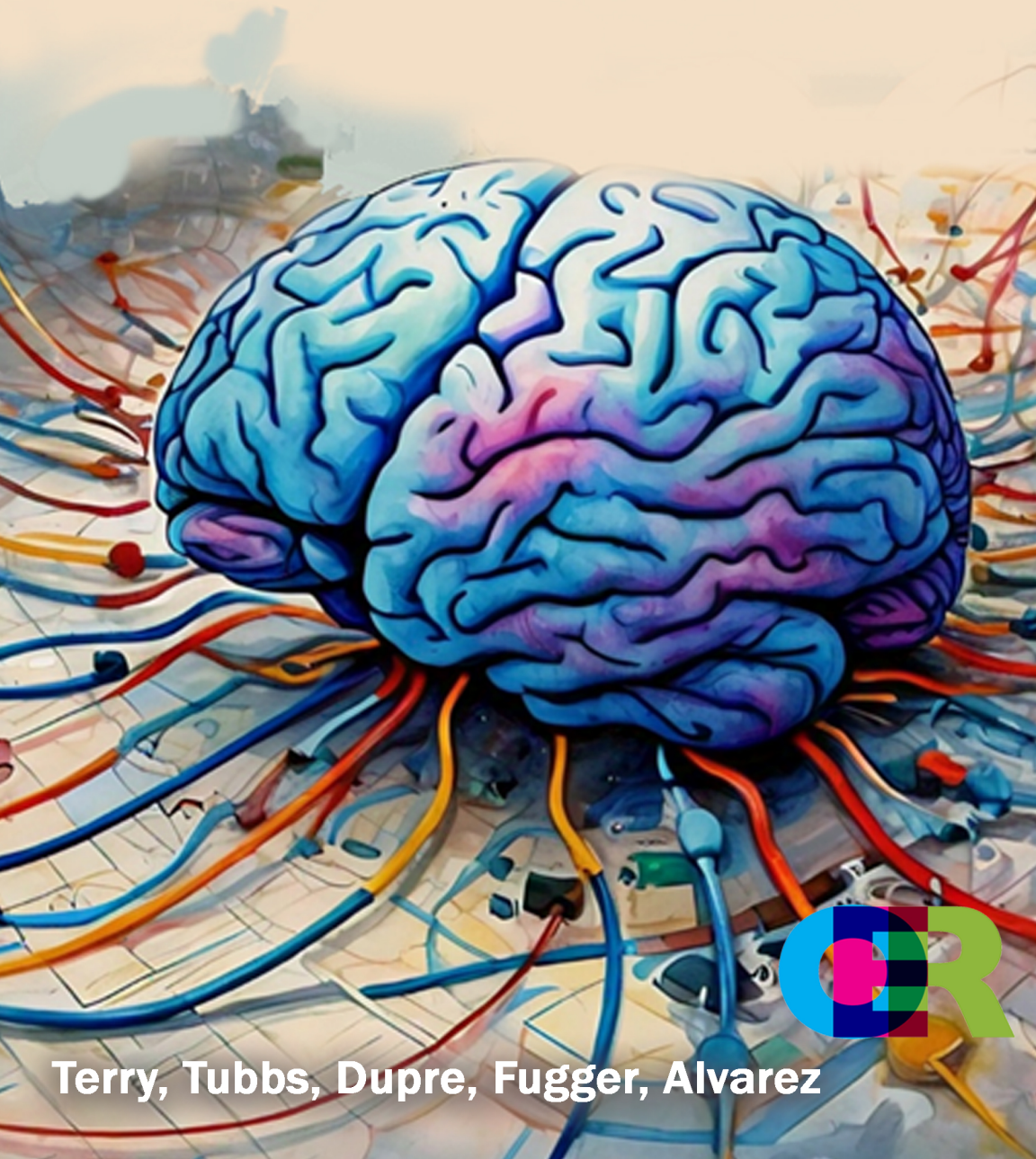


# INTRODUCTION TO NEUROENGINEERING



Terry, Tubbs, Dupre, Fugger, Alvarez





**INTRODUCTION  
TO  
NEUROENGINEERING**



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# Introduction

Neuroengineering is a rapidly evolving field at the intersection of neuroscience, engineering, and technology, aiming to develop innovative solutions to understand, interface with, and treat the nervous system. This book, "Introduction to Neuroengineering," is designed as a comprehensive resource to provide students, educators, and professionals with a thorough understanding of the foundational concepts, current technologies, and future directions in this exciting domain. By leveraging the principles of neuroengineering, we can push the boundaries of medical technology, enhance quality of life, and gain deeper insights into the workings of the human brain and nervous system.

The book is structured into several chapters, each dealing with key topics within neuroengineering. We start with the basics, such as neuron morphology and functionality, action potentials, and the nervous system. These foundational concepts set the stage for more advanced discussions on the Hodgkin-Huxley model and mathematical modeling of neurons. Understanding these principles is crucial as they form the bedrock upon which neuroengineering techniques are built.

## Chapter Breakdown

### *Neuron Morphology and Functionality*

This chapter introduces the structure and function of neurons, the fundamental units of the nervous system. It covers the different types of neurons, their roles, and how they communicate through electrical and chemical signals.

### *Hodgkin-Huxley Model and Mathematical Modeling of Neurons*

Here, we delve into the Hodgkin-Huxley model, a seminal framework for understanding the electrical characteristics of neurons. This chapter also explores various mathematical models used to simulate neuronal behavior.

## ***Neural Network Basics***

This chapter covers the basics of neural networks, including coefficient feedback and supervised and unsupervised learning. These concepts are critical for developing algorithms that mimic or interface with the human brain.

## ***EEG and MEG Hardware and Software***

Electroencephalography (EEG) and Magnetoencephalography (MEG) are non-invasive techniques for measuring brain activity. This chapter discusses the hardware and software used in EEG and MEG, noise considerations, and the advantages and disadvantages of these methods. It also explains the 10-20 system for electrode placement and how EEG data is classified into different bands and event-related potentials (ERPs).

## ***fMRI and fNIRS***

Functional Magnetic Resonance Imaging (fMRI) and functional Near-Infrared Spectroscopy (fNIRS) are imaging techniques used to measure brain activity. This chapter covers what these techniques measure, the hardware and software involved, and their advantages and disadvantages.

## ***Brain-Computer Interfaces (BCIs)***

BCIs are systems that enable direct communication between the brain and external devices. This chapter explores the main characteristics of BCIs, major applications, the current state of the art, and the pros and cons of various BCI technologies.

## ***Neurostimulation and Neuromodulation***

This chapter discusses techniques such as Transcranial Magnetic Stimulation (TMS) and Deep Brain Stimulation (DBS), including their hardware, software, advantages, disadvantages, and current technological advancements.

## ***Visual Neuroengineering***

This chapter focuses on the eye, visual nerve, and components such as cones, rods, retina, and cornea. It also covers visual-neuro diseases and their technological interventions.

## ***Psychophysics and Virtual Reality***

Psychophysics explores the relationship between physical stimuli and sensory perception. This chapter also examines the use of Virtual Reality (VR) as a tool for psychophysics and the various types of tests used in this field.

## ***Eye Tracking Technology***

Eye trackers measure eye positions and movements. This chapter discusses how eye trackers work, their effectiveness, hardware considerations, main vendors, and their advantages and disadvantages.

## ***Auditory Neuroengineering***

This final chapter covers the ear and auditory system, including nerve distributions, cochlear prostheses, and related hardware and software.

## ***Neurological Disorders and Technological Solutions***

Here, we provide a description of various neurological disorders, physiological explanations of how and why they occur, contributing factors, and current technological applications to solve these problems or improve the quality of life for affected individuals.

## **Learning Activities and Lab Examples**

In addition, each chapter includes a section dedicated to learning activities that can be implemented in classroom settings. These activities are based on the principles of collaboration, representation, safe space, and autonomy. Students can deepen their understanding of neuroengineering concepts through practical, hands-on experience by engaging in these activities.

Additionally, we propose two lab examples per chapter that apply the principles learned in each section. These lab examples involve hardware and software designed to be attainable for students at the appropriate level. These

labs reinforce theoretical knowledge and provide practical skills in using neuroengineering tools and techniques.

To further enhance the learning experience, we have accompanied this book with a GitHub repository containing self-directed lab examples. These labs are highly based on the principles of autonomy, allowing students to discover their own path of learning and apply basic principles to their interests.

In summary, "Introduction to Neuroengineering" is more than just a textbook; it is a gateway to understanding and innovating within one of modern science and technology's most dynamic and impactful fields. We hope this resource will inspire, educate, and empower you to contribute to the exciting and ever-evolving field of neuroengineering. The journey through this book is only the beginning, and we encourage you to continue exploring, experimenting, and innovating.

### ***Disclaimer***

- All graphics used in this work have been utilized with the owners' explicit permission or in accordance with the appropriate usage licenses for images.
- All graphic images presented at the beginning of each chapter were generated using ChatGPT 4.0 with the following prompt: "Create a comic book style illustration of \_\_\_\_\_, showing \_\_\_\_\_."



[https://github.com/bddupre92/Neurobook\\_BME\\_UND/](https://github.com/bddupre92/Neurobook_BME_UND/)



# Contents

<b>Introduction.....</b>	<b>2</b>
Chapter Breakdown .....	2
Learning Activities and Lab Examples .....	4
<b>Chapter 1 .....</b>	<b>16</b>
<b>Decoding Neurons: Structure, Function and Connectivity .....</b>	<b>16</b>
Introduction and Learning Objectives .....	17
Introduction to Neurons.....	17
The Action Potential.....	22
Neural Communication .....	30
The Nervous System .....	33
Chapter 1: Summary.....	37
Chapter 1: Learning activities .....	38
Learning Activity 1.1 .....	38
Learning Activity 1.2 .....	40
Learning Activity 1.3 .....	42
Chapter 1: Lab introduction .....	44
Chapter 1: Lab Example 1 .....	45
Chapter 1: Lab Example 2.....	50
<b>Chapter 2 .....</b>	<b>60</b>
<b>Hodgkin-Huxley Model, Mathematical Modeling of Neurons ....</b>	<b>60</b>
Introduction and Learning Objectives .....	61
Historical Context.....	61
Early Neuroscience: Foundations and Challenges .....	62
The Hodgkin-Huxley Model .....	65

The Hodgkin-Huxley Model's Lasting Influence .....	73
Challenges and Limitations .....	77
Chapter 2: Summary .....	84
Chapter 2: Learning activities .....	85
Learning Activity 2.1 .....	85
Learning Activity 2.2 .....	86
Learning Activity 2.3 .....	88
Chapter 2: Lab introduction .....	90
Chapter 2: Lab Example 1 .....	91
Chapter 2: Lab Example 2 .....	99
Acknowledgments .....	106
<b>Chapter 3 .....</b>	<b>108</b>
<b>Neural Networks: The Brain's Digital Doppelgangers.....</b>	<b>108</b>
Introduction and Learning Objectives .....	109
Historical Evolution of Neural Networks .....	110
Fundamentals of Neural Networks .....	113
Types of Neural Networks .....	116
Feedback Mechanisms in Neural Networks .....	121
Learning Paradigms.....	122
Real-World Example Solving Real-World Problems .....	128
Ethical, Privacy, and Security .....	132
Future Directions and Challenges .....	134
Chapter 3: Summary .....	136
Chapter 3: Learning activities .....	138
Learning Activity 3.1 .....	138

Learning Activity 3.2 .....	138
Learning Activity 3.3 .....	140
Chapter 3: Lab introduction .....	141
Chapter 3: Lab Example 1 .....	142
Chapter 3: Lab Example 2.....	147
<b>Chapter 4 .....</b>	<b>150</b>
<b>Brainwaves Unleashed: EEG and MEG .....</b>	<b>150</b>
Introduction and Learning Objectives .....	151
Classification of EEG .....	152
Components of EEG System.....	156
Chapter 4: Summary.....	175
Chapter 4: Learning activities .....	178
Learning Activity 4.1 .....	178
Learning Activity 4.2 .....	179
Learning Activity 4.3 .....	180
Chapter 4: Lab introduction .....	181
Chapter 4: Lab Example 1 .....	182
Chapter 4: Lab Example 2.....	191
<b>Chapter 5 .....</b>	<b>204</b>
<b>Illuminating the Brain: Adventures with fMRI and fNIRS .....</b>	<b>204</b>
Introduction and Learning Objectives .....	205
Functional Magnetic Resonance Imaging (fMRI).....	205
Functional Near-Infrared Spectroscopy (fNIRS) .....	219
Comparing fMRI and fNIRS .....	225
Ethical Considerations.....	226

Chapter 5: Summary .....	226
Chapter 5: Learning Activities .....	228
Learning Activity 5.1 .....	228
Learning Activity 5.2 .....	229
Learning Activity 5.3 .....	231
Chapter 5: Lab introduction .....	233
Chapter 5: Lab Example 1 .....	234
Chapter 5: Lab Example 2.....	246
Acknowledgments .....	256
<b>Chapter 6 .....</b>	<b>258</b>
<b>Bridging Minds and Machines: Brain-Computer Interfaces.....</b>	<b>258</b>
Introduction and Learning Objectives .....	259
Introduction to Brain-Computer Interfaces (BCIs) .....	259
Components of BCIs .....	262
Types of BCIs.....	271
Ethical Considerations and Future Implications .....	273
Future Directions and Challenges .....	274
Chapter 6: Summary.....	275
Chapter 6: Learning Activities .....	276
Learning Activity 6.1 .....	276
Learning Activity 6.2 .....	278
Learning Activity 6.3 .....	281
Chapter 6: Lab introduction .....	283
Chapter 6: Lab Example 1 .....	284
Chapter 6: Lab Example 2.....	289

<b>Chapter 7 .....</b>	<b>294</b>
<b>Electrifying Insights in Neurostimulation .....</b>	<b>294</b>
Introduction and Learning Objectives .....	295
Importance of Neurostimulation Technologies in Treating Neurological Disorders .....	295
Transcranial Magnetic Stimulation (TMS) .....	296
Deep Brain Stimulation (DBS).....	304
Current State of the Art .....	309
Chapter 7: Summary .....	310
Chapter 7: Learning Activities .....	312
Learning Activity 7.1 .....	312
Learning Activity 7.2 .....	315
Learning Activity 7.3 .....	317
Chapter 7: Lab introduction .....	321
Chapter 7: Lab Example 1 .....	322
Chapter 7: Lab Example 2.....	327
<b>Chapter 8 .....</b>	<b>332</b>
<b>Visual Voyage: Exploring the Wonders of the Visual System...</b>	<b>332</b>
Introduction and Learning Objectives .....	333
Anatomy of the Eye.....	333
Light Refraction and Phototransduction.....	335
Visual Pathway .....	338
Visual Disorders and Disease.....	343
Chapter 8: Summary .....	346
Chapter 8: Learning activities .....	347

Learning Activity 8.1 .....	348
Learning Activity 8.2 .....	349
Learning Activity 8.3 .....	351
Chapter 8: Lab introduction .....	353
Chapter 8: Lab Example 1 .....	354
Chapter 8: Lab Example 2.....	361
<b>Chapter 9 .....</b>	<b>364</b>
<b>The Eyes Have it: Unlocking Secrets with Eye Trackers .....</b>	<b>364</b>
Introduction and Learning Objectives .....	365
Review of Anatomy Applied to Eye Tracking .....	365
Eye Tracking Technology .....	366
Performance and Limitations .....	373
Applications in Research.....	374
Available Products on the Market .....	374
Emerging Trends in Eye Tracking Tech .....	377
Challenges and Future Directions .....	378
Chapter 9: Summary.....	379
Chapter 9: Learning activities .....	380
Learning Activity 9.1 .....	380
Learning Activity 9.2 .....	382
Learning Activity 9.3 .....	384
Chapter 9: Lab introduction .....	386
Chapter 9: Lab Example 1 .....	387
Chapter 9: Lab Example 2.....	395
<b>Chapter 10 .....</b>	<b>404</b>

**Mind Games: The Worlds of Psychophysics and Virtual Reality**  
..... **404**

    Introduction and Learning Objectives ..... 405

    Introduction to Psychophysics..... 405

    Fundamentals of Psychophysical Methods ..... 406

    Types of Psychophysical Tests..... 411

    Current Trends and Future Directions in Psychophysics ..... 413

    Future Work ..... 417

    Chapter 10: Summary..... 417

    Chapter 10: Learning activities ..... 420

    Learning Activity 10.1 ..... 420

    Learning Activity 10.2 ..... 423

    Chapter 10: Lab introduction ..... 426

    Chapter 10: Lab Example 1 ..... 427

    Chapter 10: Lab Example 2..... 431

**Chapter 11 ..... 442**

**Tuning In: Exploring the Marvels of The Auditory System..... 442**

    Introduction to the Auditory System ..... 443

    Overview of Auditory System Function ..... 444

    The Ear Anatomy ..... 444

    Sound Characteristics ..... 448

    Mechanism of Hearing ..... 449

    Auditory Nerves and Processing ..... 450

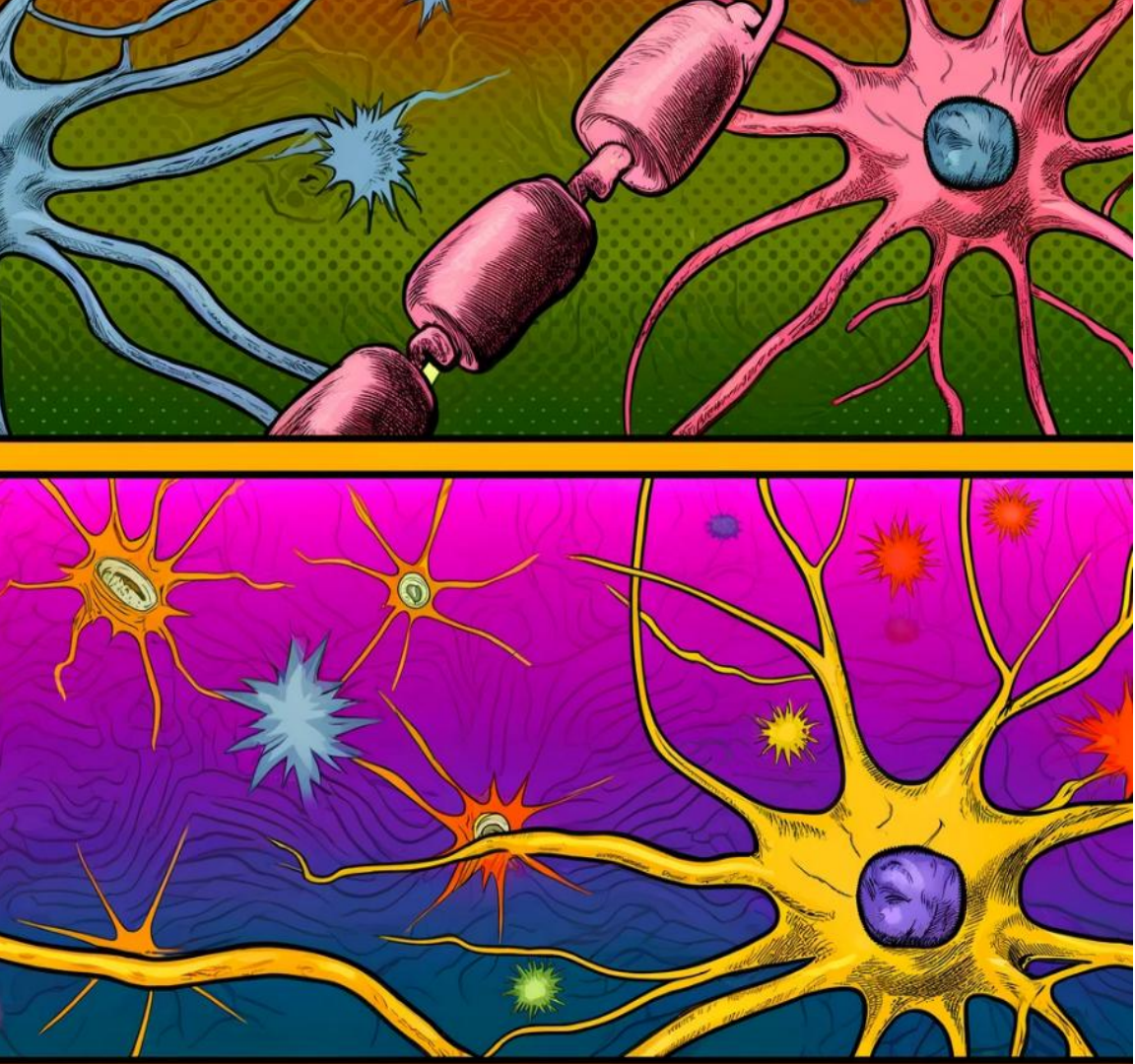
    Hearing Loss..... 452

    Hearing Loss Treatment ..... 455

Neuroengineering Applications.....	457
Chapter 11: Summary.....	458
Chapter 11: Learning Activities .....	459
Learning Activity 11.1 .....	459
Learning Activity 11.2 .....	461
Learning Activity 11.3 .....	463
Chapter 11: Lab introduction .....	466
Chapter 11: Lab Example 1.....	467
Chapter 11: Lab Example 2.....	470
<b>Chapter 12 .....</b>	<b>478</b>
<b>The Battle Frontier: Fighting Neurological Disorders .....</b>	<b>478</b>
Chapter Introduction and Learning Objectives .....	479
Detailed Disorder Profiles .....	480
Parkinson's Disease .....	481
Autism Spectrum Disorder (ASD) .....	484
Multiple Sclerosis (MS) .....	485
Amyotrophic Lateral Sclerosis (ALS).....	487
Dementia .....	489
Huntington's Disease .....	491
Impact on Society .....	492
Technological Interventions in Neurological Disorders .....	494
Future Directions .....	500
Chapter 12: Summary.....	500
Chapter 12: Learning activities .....	502
Learning Activity 12.1 .....	502

Learning Activity 12.2 .....	503
Chapter 12: Lab introduction .....	505
Chapter 12: Lab Example 1 .....	506
Steps .....	506
Chapter 12: Lab Example 2.....	515
Statistical Analysis .....	520
Script Structure.....	521
Summary .....	523
<b>General Conclusion.....</b>	<b>525</b>
<b>Acknowledgments .....</b>	<b>528</b>
<b>About the authors .....</b>	<b>529</b>
<b>References .....</b>	<b>532</b>





## **Chapter 1**

# **Decoding Neurons: Structure, Function and Connectivity**

# Introduction and Learning Objectives

Hello reader, in this first chapter, we will explore the fundamental building block of the brain: neurons. This chapter will provide a foundational understanding of neurons by examining their structure and function. Then, the chapter will discuss the mechanisms behind how neurons communicate and the intricacies involved in neural processing. The chapter ends by discussing the organization of the central and peripheral nervous systems, highlighting the functional divisions. This foundational knowledge is crucial for anyone aiming to innovate in the field of neural engineering, as it provides the background needed to develop new technologies and interventions. By the end of this chapter, you will be able to:

1. *Describe neuron morphology, explain how each component contributes to neural signaling, and identify different types of neurons.*
2. *Explain the process of action potential generation and propagation.*
3. *Understand the organization of the central and peripheral nervous system.*

## Introduction to Neurons

### *Definition and Morphology of Neurons*

Our entire body is composed of cells, and in the brain, these cells are called neurons. The neurons are the fundamental units of the brain and nervous system and are responsible for transmitting information throughout the entire body. These signals control everything in our body, from basic reflexes to complex thoughts, emotions, and behaviors. The neurons' anatomical structure, or morphology, is important because it is designed to transmit these signals as fast and efficiently as possible and is dictated by the specific function that neurons are supposed to carry out. The main morphological features of a neuron are the dendrites, the soma or cell body, the axon, the myelin sheath, and the axon terminals (Fig. 1.1 [1], [2]).

The dendrites are the first stop for neurons to transmit signals through the body. The dendrites are branching processes that extend from the soma of the neurons. These branching-like structures are sometimes referred to as dendritic trees or dendritic arbors due to their structures resembling those of tree branches. The complexity of the branching of the dendrites can vary depending on the type of neuron. The function of the dendrites is to receive signals from other neurons and transmit those signals to the soma. The dendrites are crucial

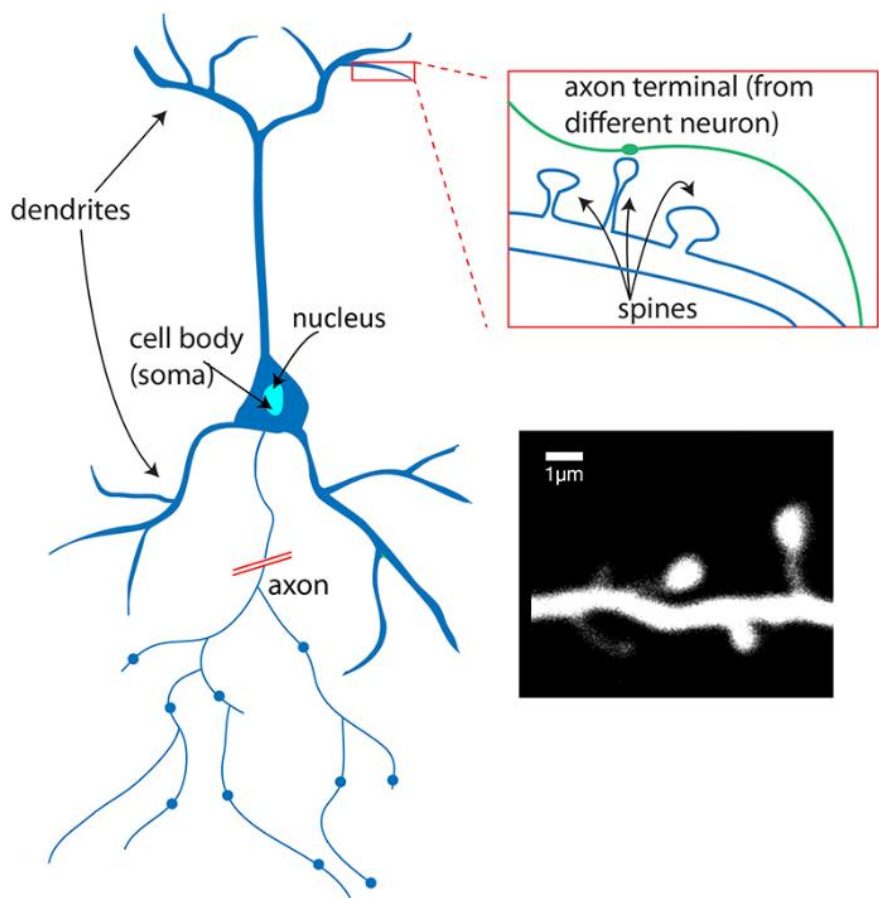


Figure 1.1: Neuron Morphology (left) with close up of axon terminals (top right) and segment of dendrite (bottom left) [1],[2]

for integrating signal inputs to determine the neuron output. The dendrites can be thought of as an antenna on a satellite dish. Like how antennae receive signals from different sources, the dendrite receives many incoming signals from various other neurons and relays those signals to the soma.

Once the signal travels down the dendrites, it will reach the soma. The soma, the neuron's cell body, contains the organelles typically found in cells, such as the nucleus, the endoplasmic reticulum, and mitochondria. These organelles maintain the health of the cell and integrate all the signals received from the dendrites to determine the neuron's output. The soma can be considered a company's central operation office. Many different players, in this case, organelles, are working together to control activities and make decisions to direct actions. Once the soma can integrate the signals received from the dendrites, the soma then sends the output signal to the axon.

The axon is a long projection whose length can vary from a short length of less than a millimeter to a meter or more. The axon originates from a specialized part of the soma called the axon hillock. This specialized part of the soma is crucial because it is where the neuron initiates action potentials, which we will discuss later in this chapter. The axon transmits the signals away from the soma to other neurons in the body, whether in the brain, muscles, or glands. The axon is essential for communicating the signals across various distances in the body. This part of the neuron can be thought of as a delivery truck that must travel to deliver packages. In this case, the package is an electrical signal, and the recipient is various body parts. The axon has multiple other structures to ensure its signal can be delivered as fast as possible. These structures include the myelin sheath and the nodes of Ranvier.

The myelin sheath is a fatty insulating layer formed by glial cells. Oligodendrocytes are the glial cells that myelinate the axons of neurons in the central nervous system (CNS). In contrast, Schwann cells are the glial cells that myelinate the axons of neurons in the peripheral nervous system (PNS). Diseases such as multiple sclerosis, which will be discussed more in Chapter 12, can lead to the destruction of these glial cells, resulting in demyelination of the axon and the axon's inability to transmit electrical signals to other neurons. The function of the myelin sheath is to increase the speed of the signal

as it travels down the axon. The axon can speed up this transmission using the nodes of Ranvier, which are gaps in the myelin sheath where the axonal membrane is exposed. When the signal travels down the axon, it “jumps” from one node of Ranvier to the next. This “jumping” allows for the signal to transmit efficiently and quickly. The process of the signal moving down the axon in this way is called saltatory conduction. The myelin sheath can be thought of as the insulation of electrical wires. Just as the wire insulation speeds up electrical transmission in a circuit, the myelin sheath insulates the axon to speed up neural signal transmission. Ranvier's nodes can be considered stepping stones in a stream that allows you to jump from stone to stone across a stream. The nodes will enable the signal to “jump” from one node to the next along the axon. Once the signal jumps down the nodes of Ranvier, it reaches its destination at the axon terminals, also known as the terminal boutons or synaptic boutons. This part of the neuron transmits the signal to the next neuron. The axon terminals contain additional structures, such as synaptic vesicles and mitochondria, which support signal transmission. This will be discussed in more detail later in this chapter.

While all neurons typically have the same morphology, their organization can look very different. These differences end up producing various types of neurons.

## ***Types of Neurons***

Neurons can be classified based on their structure and function. When looking at how the anatomical structures of neurons are organized, they can be classified as unipolar, bipolar, or multipolar, as depicted in Fig. 1.2 [3]. Unipolar neurons exhibit one single process extending from the soma. Bipolar neurons have two processes, typically one axon and one dendrite, that extend in opposite directions from the cell body. Finally, multipolar neurons, the most common type, have one axon extending from one end of the soma and several dendrites extending from the other.

These differences in structure give insights into the neuron's function. For instance, unipolar neurons are typically found in neurons that function as sensory neurons. Sensory neurons, called afferent neurons, transmit sensory information to the central nervous system (CNS). For

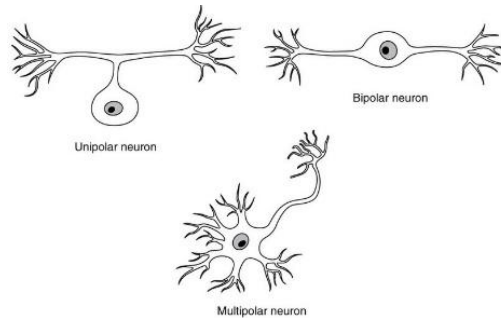


Figure 1.2: Types of Neurons [3]

example, dorsal root ganglion neurons are unipolar sensory neurons that take sensory inputs such as pain, temperature, and proprioception from peripheral tissues to the CNS. In these neurons, a process comes from the soma that bifurcates (splits), with one branch extending to the sensory receptors in the skin or other tissues and the other branch extending to the spinal cord. When a unipolar neuron bifurcates, such as those for the DRG, they are called pseudo unipolar neurons. The structure of these neurons is essential for them to efficiently transmit sensory information over long distances. Not all sensory neurons are unipolar; some can be bipolar. However, sensory neurons are not usually multipolar.

The nervous system also employs motor neurons and interneurons. Motor neurons, or efferent neurons, take signals from the CNS to target cells in muscles and glands to carry out actions. Motor neurons are typically multipolar neurons with multiple processes extending to other neurons and target cells. The multipolar structure of these neurons is crucial for allowing them to receive inputs from various sources and integrate them to control muscles efficiently. The nervous system uses interneurons to link sensory and motor neurons to communicate signals from the CNS to the peripheral nervous system (PNS). Interneurons are also typically multipolar, allowing them to receive sensory information, integrate it, and transmit an output signal to motor neurons. Understanding the morphology of neurons and their structural

diversity is foundational knowledge for understanding the dynamic process of neuronal communication.

# **The Action Potential**

## ***Membrane Potential***

The membrane potential in a neuron is the electrical potential difference across the cell membrane. This potential is created due to an unequal distribution of charged ions between the cell's intracellular (inside) and extracellular (outside) environments. The membrane potential is crucial in the neuron's ability to generate and propagate electrical signals, called action potentials. The membrane has a resting potential of -70 millivolts (mV). This negative potential is established and maintained by ion concentration gradients, membrane permeability, and the sodium-potassium pump.

## ***Concentration Gradients***

A concentration gradient is established when a solute's concentration varies across different regions in a solution. When discussing neurons, our solutes are ions, the solution is the body's fluids, and the regions are the intracellular and extracellular fluids. The cell's phospholipid bilayer acts as the membrane separating these regions. The concentration gradient in the neuron is due to a difference in ion concentrations and the membrane's selective permeability. The ions that are primarily involved in the creation of this gradient are sodium ( $\text{Na}^+$ ), potassium ( $\text{K}^+$ ), chloride ( $\text{Cl}^-$ ), and calcium ( $\text{Ca}^{2+}$ ).  $\text{Na}^+$  and  $\text{Ca}^{2+}$  ions have higher concentrations outside the cell than inside, whereas  $\text{K}^+$  and  $\text{Cl}^-$  have higher concentrations inside the cell.

## ***Permeability***

The cell membrane of the neuron is selectively permeable. This means the membrane regulates the passage of certain substances across it, which is essential for maintaining homeostasis. The membrane's permeability is established due to its structure. The cell membrane is a phospholipid bilayer where two layers of phospholipids containing a hydrophilic head and a hydrophobic tail come together. The hydrophobic tails make up the interior of the bilayer and act as a barrier for water-soluble substances, while the

hydrophilic heads make up the exterior of the bilayer and interact with the extracellular and intracellular environments. The membrane is composed of proteins, cholesterol, and carbohydrate chains. Integral proteins, especially ion channels embedded in the bilayer, facilitate selective permeability through passive and active transport mechanisms. This will be discussed in more detail later in the chapter.

### ***Sodium Potassium Pump***

The sodium-potassium ATPase pump is a membrane protein that uses energy from adenosine triphosphate (ATP) to transport ions against their concentration gradient from an area of low concentration to an area of high concentration. Specifically, this pump moves  $\text{Na}^+$  ions out of the cell and  $\text{K}^+$  ions into the cell, transporting them against their concentration gradients. The transport of these ions is essential for maintaining their concentration gradient inside and outside the cell. The pump operates through a cycle that involves binding and moving ions across the membrane. First, the pump binds three  $\text{Na}^+$  from inside the cell and then hydrolyzes ATP to adenosine diphosphate (ADP). This hydrolysis breaks one of the phosphate bonds on the ATP, releasing energy in phosphorylation. Phosphorylation adds a phosphate group to the pump, causing a conformational change in the pump allowing it to transport  $\text{Na}^+$  ions into the extracellular space. The pump binds two  $\text{K}^+$  ions from the extracellular fluid in this new conformation. It uses dephosphorylation to undergo another conformation change, returning the pump to its original shape and exposing the  $\text{K}^+$  to the intracellular fluid, where it can be released. Since the pump uses energy to move ions from one side of the membrane to the other, it is called active transport.

Now that you have established the foundation of the membrane potential, we can discuss how ion channels orchestrate the flow of these ions across the membrane to drive dynamic changes in the electrical charge necessary for neurons to communicate with one another.

### ***Ion Channels***

The proteins embedded in the membrane make up ion channels where ions can enter or leave the cell. There are different channels, such as voltage-gated ion

channels, ligand-gated channels, mechanically-gated channels, and leak channels. Voltage-gated channels open in response to changes in the membrane potential. Ligand-gated channels open in response to a molecule (ligand) binding. Mechanically-gated channels respond to mechanical stimuli such as stretching or pressure changes. Leak channels are always open, allowing ions to move down their concentration gradients across the membrane.

Voltage-gated ion channels are crucial for neural communication and undergo a conformation change in response to electrical stimuli, allowing them to open to allow ions to pass through. These channels have specific characteristics that make them selective to ions, which only allows specific ions to pass through. For example, there is a voltage-gated ion channel that is selective to  $\text{Na}^+$  and selective to  $\text{K}^+$ . The ion channel pore size can determine the selectivity of these channels. The  $\text{K}^+$  channel is narrower than the  $\text{Na}^+$  channel and wouldn't be big enough for the larger  $\text{Na}^+$  ion to pass through. Additionally, the channels are lined with specific amino acids that create a charge that will favor the passage of particular ions. For example, the  $\text{Na}^+$  channels have a negatively charged amino acid near the entrance to attract the positively charged  $\text{Na}^+$  ions. The channel selectivity ensures that the appropriate ions can pass through at the correct times for the neurons to communicate by generating action potentials. The movement of the ions down these channels without energy is a type of transport called passive transport. In this case, this type of passive transport is called facilitated diffusion. The ions can travel down the channels because they are moving down their concentration gradient from an area of high concentration to an area of lower concentration. Other examples of channels that use passive transport are ligand-gated channels and leak channels. In these channels, the ions' concentration gradient determines the rate at which passive transport occurs and does not require energy [4].

## ***Action Potential Phases***

The way that neurons can communicate with each other is by generating action potentials. The action potential is an electrical event in neurons involving rapid changes in potential across the neuron's cell membrane. The action potential

has three distinct sequential phases: depolarization, repolarization, and the refractory period. These phases can be seen in Fig. 1.3 [5].

### ***Depolarization***

The neurons start at a resting potential of  $-70$  mV due to unequal ion distributions inside and outside the cell. The neuron membrane contains ligand-gated  $\text{Na}^+$  channels that open once the neuron receives an excitatory electrical impulse, called excitatory postsynaptic potential (EPSP), from another neuron [6]. Once an excitatory neurotransmitter binds to these gate channels, they open, allowing  $\text{Na}^+$  to influx (enter) the cell. As  $\text{Na}^+$  continues to enter the cell, the membrane potential becomes more positive. An action potential will occur once enough  $\text{Na}^+$  enters the cell to reach a threshold of  $-55$  mV.

The action potential is an all-or-nothing event. If the neuron does not receive sufficient EPSP to reach the threshold, an action potential will not occur, and the membrane potential will return to resting potential. These failed action potentials are referred to as “Failed Initiations.” Once the threshold is met, voltage-gated  $\text{Na}^+$  channels open, allowing more  $\text{Na}^+$  to influx into the cell to reach a membrane potential of around  $40$  mV. At this point in the action potential, the  $\text{Na}^+$  channels begin to close, and voltage-gated  $\text{K}^+$  opens.

### ***Repolarization***

The closure of the  $\text{Na}^+$  channels ensures that no more  $\text{Na}^+$  enters the cell, and the opening of the  $\text{K}^+$  channels allows  $\text{K}^+$  ions to efflux out of the cell. The efflux of  $\text{K}^+$  leads to the membrane potential getting more negative to try and restore the membrane potential to its resting value. The  $\text{K}^+$  channels can be opened for a prolonged time, causing excessive amounts of  $\text{K}^+$  to leave the cell. This causes the membrane potential to become more negative than the resting potential, called hyperpolarization. The voltage-gated potassium channels eventually close and restore resting membrane potential.

***Refractory Period***

The inactivation of voltage-gated sodium channels and the hyperpolarization of voltage-gated potassium channels results in a refractory period. This feature of the action potential may seem counterintuitive to ensuring signals are transmitted quickly. Still, it is essential to ensure that action potentials travel in one direction down the axon and helps regulate the frequency and timing of neuron firing.

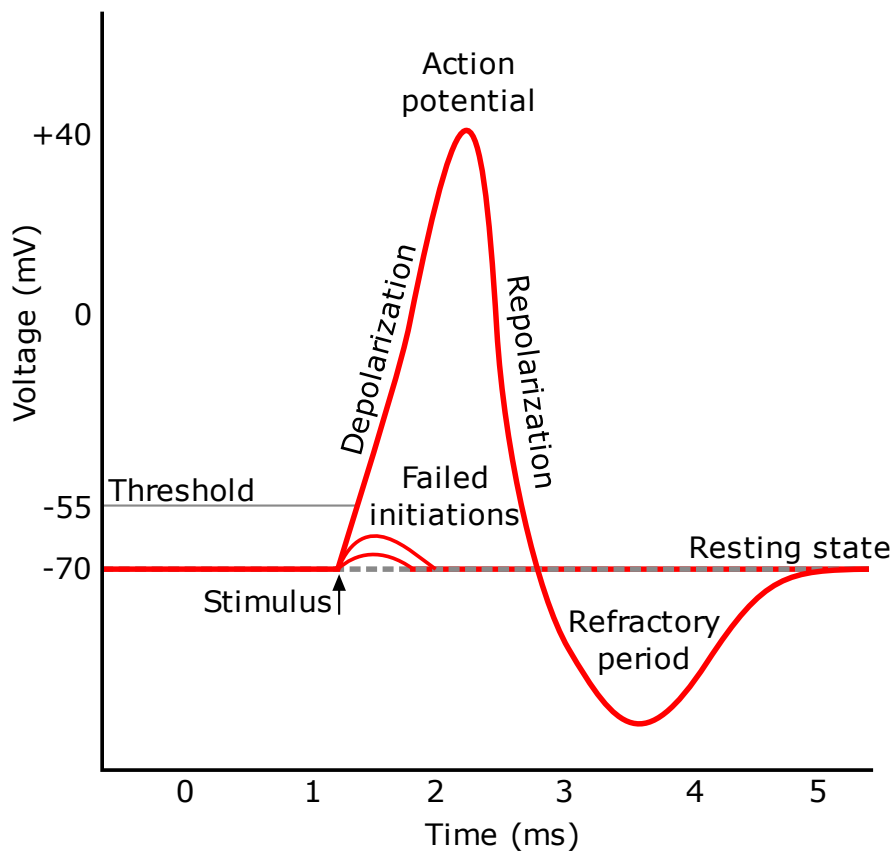


Figure 1.3: Diagram of Action Potential [5]

The rise and fall of the influx or efflux of specific ions during the action potential are driven not only by the opening and closing of the channel but also by the ion's equilibrium potential. The equilibrium potential of an ion is the membrane potential at which the net flow of that ion across the membrane is zero. The concentration gradient and the electrical gradient across the membrane determine it. When the membrane potential is equal to the equilibrium potential of a particular ion, there is no net movement of that ion across the membrane. Therefore, during the action potential, as the membrane potential changes, ions move in or out of the cell depending on whether the membrane potential is above or below their respective equilibrium potentials. This movement of ions contributes to the rise and fall of the action potential, allowing for the transmission of electrical signals along the neuron. The Nernst Equation can determine the equilibrium potential of the ions for a given ion across a semipermeable membrane[7]. The Nernst equation is expressed as:

$$E_{ion} = \frac{RT}{zF} \ln \left( \frac{[ions_{out}]}{[ions_{in}]} \right) \quad (1.1)$$

Where  $E_{ion}$  is the equilibrium or Nernst potential of the ion in volts, R is the ideal gas constant (8.314 J/Kmol), T is temperature in Kelvin, z is the charge of the ion, F is the Faraday constant (96,485 A/mol), and  $[ions_{out}]$  and  $[ions_{in}]$  are the concentrations of ions outside and inside the cell, typically measured in millimoles per liter (mm/L). The Nernst equation is relevant for determining neurons' resting potential and action potentials' generation. During the action potential, changes in the permeability of the ions across the membrane lead to shifts in the membrane potential. This equation can help predict the membrane potential when each ion will be in equilibrium during different phases. This helps to provide insights into mechanisms of neuronal excitability and signal propagation. However, the Nernst equation can only determine the membrane potential based on a single ion species. The Goldman Equation determines the permeability of multiple ions and their concentration gradients. This equation describes the resting membrane potential of a cell based on the permeability of multiple ions and

is expressed as:

Where  $V_m$  is the membrane potential,  $R$ ,  $T$ , and  $F$  represent the same parameters as the Nernst equation,  $P_{K^+}$ ,  $P_{Na^+}$ , and  $P_{Cl^-}$  are the permeability of the membrane to that ion, and  $[K^+]$ ,  $[Na^+]$ , and  $[Cl^-]$  are the concentration of the ion. The Goldman Equation provides a more accurate representation of the membrane potential since it considers multiple ions with different permeability and accounts for complex interactions between ions and how they influence the membrane potential.

$$V_m = \frac{RT}{F} \cdot \ln \left( \frac{P_{K^+} + [K^+]_{out} + P_{Na^+} + [Na^+]_{out} + P_{Cl^-} - [Cl^-]_{out}}{P_{K^+} + [K^+]_{in} + P_{Na^+} + [Na^+]_{in} + P_{Cl^-} - [Cl^-]_{in}} \right) \quad (1.2)$$

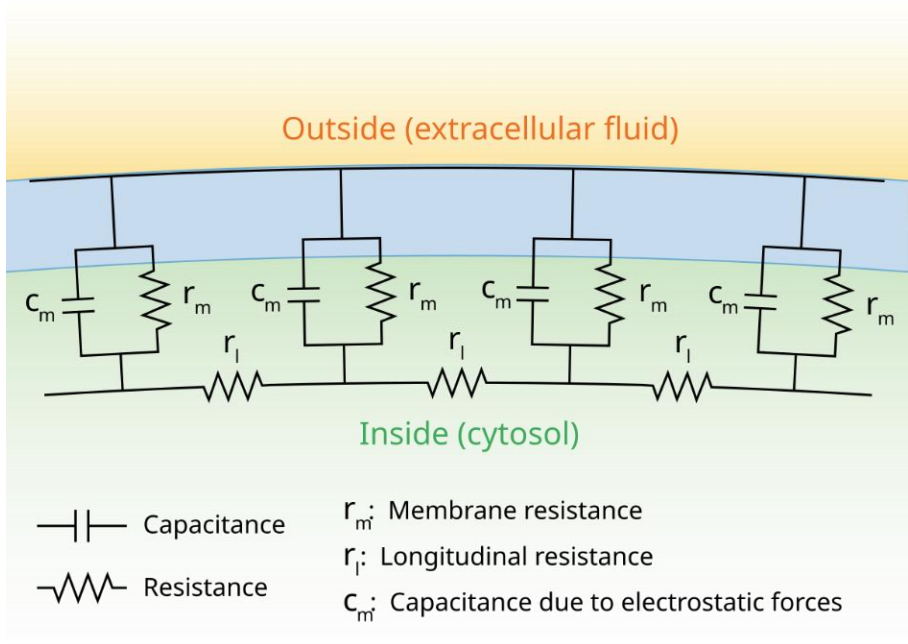


Figure 1.4: The Cable Model [10]

## ***Action Potential Propagation***

After the action potential is initiated at the axon hillock, the adjacent region of the axon's membrane is then depolarized, initiating another action potential. This sequential depolarization and repolarization occur along the entire length of the axon, propagating the action potential.

Section 1.1 of this chapter discussed saltatory conduction and how this signal propagates by jumping from one node of Ranvier to the next. Several factors can influence the speed of the signal's propagation down the axon, such as myelination, the diameter of the axon, and temperature. As the diameter of the axon gets larger, it offers less resistance to ion flow and will produce faster conduction velocities compared to smaller-diameter axons. Higher temperatures will also increase the speed of the action potential propagation by accelerating the rate at which the ion channels open and close [8]. Just as we can use the Nernst equation to understand the equilibrium potentials of ions computationally, we can use the Cable Theory and Model to mathematically represent and understand signal propagation along the axon.

### ***Cable Theory and Model***

$$\frac{\partial V}{\partial t} = \frac{1}{r_m \cdot c_m} \cdot \frac{\partial V^2}{\partial x^2} - \frac{1}{r_m \cdot r_l} \cdot \frac{\partial V}{\partial x} \quad (1.3)$$

The Cable Theory is a framework for understanding how the action potentials' electrical signals propagate along the axon's length.

This theory models the neuronal axon as a cylindrical cable with electrical properties that govern signal transmission. The theory also highlights that space and time play a role in determining the speed and attenuation of signal propagation along an axon [9]. The theory derives the cable model (Fig. 1.4 [10]) and the cable equation, which is expressed as:

Where  $V$  is the membrane potential in volts as a function of position,  $x$ , along the neuron, and time,  $t$ , terms  $r_m$  and  $c_m$  are the membrane resistance and capacitance per unit area, respectively. Term  $r_l$  is the longitudinal resistance per unit length.

Term

$$\frac{\partial V^2}{\partial x^2}$$

is the rate of change of the membrane potential concerning time and is the second derivative of the membrane potential with respect to position. This equation describes how the membrane potential changes as the signal propagates down the axon over space and time. The equation accounts for the neuron's electrical properties and ion flow's longitudinal resistance. The cable model determines and predicts the spatial (space/position) and temporal (time) dynamics of action potential propagation.

Now that we have understood how neurons can create action potentials and how those action potentials travel down the axon, we will explore how these concepts come together to generate neural communication.

## Neural Communication

Once the electrical signal travels down the axon, it will reach the axon terminal containing synapses. At these synapses, the neuron can either communicate using an electrical synapse or a chemical synapse.

### *Synaptic Transmission*

Electrical synapses, or gap junctions, connect adjacent neurons that allow for direct electrical communication. In these synapses, the electrical signal is transmitted through direct electrical coupling through gap junction channels formed by connexin proteins. These proteins span the membranes of the two neurons, creating a direct pathway from one neuron to the next. Gap junctions provide a fast and efficient way to transmit signals between neurons and are involved in sensory processing and motor control.

On the other hand, a chemical synapse involves a more specialized junction between the neurons, which transmit signals through the release of chemical messengers called neurotransmitters. These synapses have several key components that are all important for proper signal transmission. The first component is the presynaptic terminal. This is where the signal has already traveled down the axon of a presynaptic neuron and is ready to send the signal

to the next neuron. The presynaptic terminal contains synaptic vesicles filled with neurotransmitters and voltage-gated calcium channels on its membrane. In between the two neurons is a narrow space called the synaptic cleft. The cleft acts as a physical barrier that neurotransmitters must cross to transmit signals from the presynaptic to the postsynaptic neuron. The neurotransmitters bind to protein receptors on the postsynaptic neuron. Chemical synapse transmission occurs by the following steps:

1. The presynaptic neuron receives an action potential at the axon terminal, depolarizing the membrane.
2. Voltage-gated calcium channels in the membrane open.
3. Calcium ions influx into the presynaptic neuron.
4. Calcium binds to the synaptic protein synaptotagmin that anchors the vesicle to the membranes.
5. The Calcium-bound synaptotagmin interacts with SNARE proteins on the vesicle and presynaptic membrane. This causes a conformational change in the SNARE complex.
6. The vesicles, filled with neurotransmitters, will move toward and dock at the presynaptic membrane.
  - a. The vesicles undergo exocytosis at the presynaptic membrane and release neurotransmitters into the synaptic cleft.
  - b. Neurotransmitters diffuse across the synaptic cleft and bind to protein receptors on the postsynaptic neuron.
  - c. The receptor undergoes a conformation change, leading to the opening or closing of ion channels and changes in the postsynaptic membrane potential.

Chemical synapses are dynamic and plastic, allowing fine-tuning signal transmission in response to environmental stimuli [11]. They are essential for various nervous system functions, such as sensory processing, motor control, and memory. Many different neurotransmitters and receptors have roles in orchestrating signal transitions across chemical synapses.

## ***Neurotransmitter and Receptors***

Neurotransmitters are chemical messengers that transmit signals across the chemical synapse and influence the activity of the postsynaptic neuron. Neurotransmitters interact with their specific receptors on the postsynaptic membrane to trigger changes in the membrane potential to either excite or inhibit neuron activity. When a neurotransmitter excites a neuron, it will deliver an excitatory postsynaptic potential (EPSP) that will depolarize the neuron, bringing it closer to the threshold to trigger an action potential. When a neurotransmitter inhibits a neuron, it will deliver an inhibitory postsynaptic potential (IPSP) that will hyperpolarize the neuron, bringing it closer to resting potential and making it harder to trigger an action potential [6]. When signals are delivered rapidly from one presynaptic neuron, the signals are summated in a temporal summation process. If signals are supplied simultaneously but from different presynaptic neurons, the signals will still summate in a process called spatial summation. Several types of neurotransmitters and their receptors deliver either EPSP or IPSP. Here, we will discuss the most common ones.

### ***Glutamate***

Glutamate is the primary excitatory neurotransmitter in our central nervous system (CNS) and plays a critical role in synaptic transmission, learning, and memory. The two glutamatergic (meaning a receptor or system that involves glutamate) are the AMPA ( $\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid) and NMDA (N-methyl-D-aspartate) receptors.

### ***GABA (Gamma-Aminobutyric Acid)***

GABA is the primary inhibitory neurotransmitter in the CNS, mediating synaptic inhibition and regulating neuronal excitability. Its receptors are GABA-A and GABA-B.

### ***Dopamine***

Dopamine is critical in several processes, such as reward-motivated behavior, motor control, and cognition. Depending on its receptor subtype, it can deliver either EPSPs or IPSPs. For instance, the D1-like receptors, which are receptors D1 and D5, are typically excitatory and often associated with reward,

motivation, and motor control. D2-like receptors, which are receptors D2, D3, and D4, can deliver either signal type depending on where they are in the brain and under the context in which they are being used.

### ***Serotonin***

Serotonin effects can vary widely depending on the receptor used and the brain region in which it is used. Some of its receptors mediate EPSPs and some IPSPs. Serotonin is crucial in mood, appetite, sleep, and other physiological processes. Its receptors are the 5-HT receptors.

### ***Acetylcholine***

Acetylcholine's effects are also diverse depending on the receptor and location. In the CNS, it acts primarily as an excitatory neurotransmitter, while in the peripheral nervous system (PNS), it can deliver EPSPs or IPSPs. Its receptors are the nicotinic and muscarinic receptors.

Now that we have established the different types of neural signal transmission and explored the various neurotransmitters contributing to that transmission, we will turn to the nervous system's boundary organization and function, where signal transmission integrates to produce our complex behaviors and physiological processes.

## **The Nervous System**

The nervous system comprises two main components: the central nervous system (CNS) and the peripheral nervous system (PNS). Each plays a distinct but interconnected role in regulating and coordinating all bodily functions and responses.

### ***Central Nervous System (CNS) and Peripheral Nervous System (PNS)***

The CNS holds the brain and spinal cord and is the main control center for processing and interpreting sensory information, making decisions, and sending commands. The brain is the most complex organ in our bodies and is responsible for everything from simple things like our hearts beating to complex thoughts and emotions. The brain consists of various regions, such as

the brainstem, cerebellum, diencephalon, and cerebrum, each with different functions and responsibilities (Fig. 1.5 [12], [13]).

### ***Brainstem***

The brainstem consists of the midbrain, pons, and medulla oblongata and connects the brain to the spinal cord. It also controls vital functions such as heart, breathing rate, and blood pressure.

### ***Cerebellum***

The cerebellum is beneath the cerebrum and is crucial for balance, coordination, and voluntary movements. It ensures that our movements are smooth and precise.

### ***Diencephalon***

The diencephalon is a region that includes the thalamus and the hypothalamus. The thalamus is the relay station that transmits sensory and motor signals to the cerebrum to regulate sleep and alertness. The hypothalamus regulates

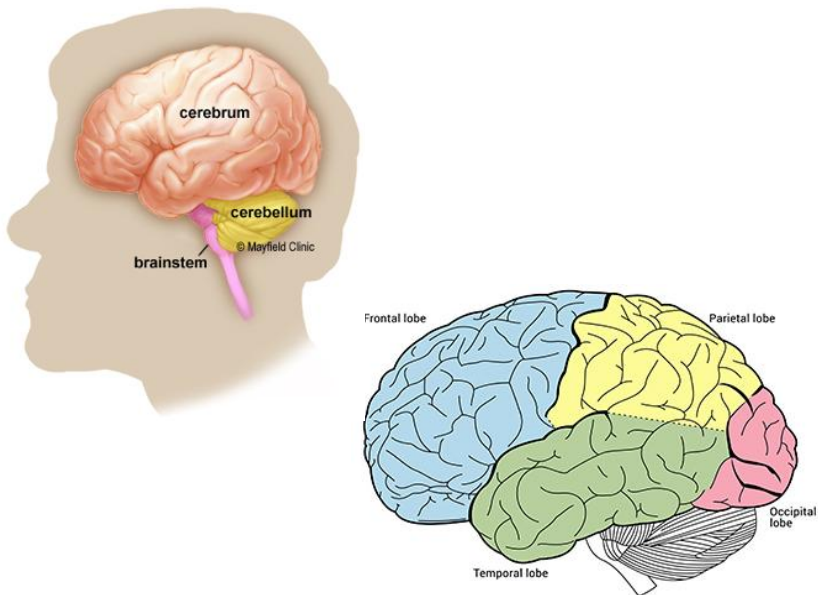


Figure 1.5: The Four Subdivisions of the Brain (left) and the Regions of the Brain (right) [12],[13]

hunger, thirst, temperature control, and circadian rhythm. It also controls the pituitary gland.

### ***Cerebrum***

The cerebrum is the largest part of the brain and is responsible for higher functioning, such as thoughts, memories, emotions, and voluntary movements. It is divided into two hemispheres, which are divided into four lobes: the frontal, parietal, temporal, and occipital lobes. It is made up of both gray and white matter. The white matter primarily comprises the myelinated axons of the neurons, while the gray matter is composed of the soma, dendrites, unmyelinated axons, glial cells, and capillaries.

The spinal cord acts as a conduit for signals between the brain and the rest of the body and is involved in reflexes and execution of simple motor commands. It is a cylindrical structure that extends from the base of the brain down through the vertebral column. It is the main pathway for transmitting information between the brain and the rest of the body and is organized into distinct regions and structures (Fig. 1.6 [14]).

### ***Gray Matter***

The gray matter is in the center of the spinal cord and contains neuron cell bodies, dendrites, and unmyelinated axons. It is organized in the dorsal, ventral, and lateral horns.

## ***White Matter***

The white matter surrounds the gray matter and consists of myelinated axons forming ascending and descending tracts. These tracts allow communication between the brain and the different parts of the spinal cord.

## ***Spinal nerves***

Thirty-one pairs of spinal nerves emerge from the cord and carry sensory information from the CNS to motor command to the peripheral tissues.

The structure of the CNS allows for vast amounts of information to be processed as fast and as efficiently as possible to coordinate behaviors and maintain vital physiological processes. This organization is needed for the proper functioning of the nervous system.

The PNS connects the CNS to the rest of the body and is divided into two subdivisions: the somatic and autonomic nervous systems. The somatic nervous system controls our voluntary movements by sending motor commands from our CNS to the skeletal muscles. It also sends sensory information from the skin, muscles, and sensory organs to the CNS to perceive touch, pain, temperature, and body position. The autonomic nervous system regulates involuntary functions such as heart rate, digestion, respiratory rate, and blood pressure. This system is further divided into two branches: the sympathetic and parasympathetic nervous systems. The sympathetic nervous system controls our fight or flight response to prepare our bodies for stress or emergencies. The parasympathetic nervous system controls our rest and digestion response to help maintain baseline conditions or homeostasis.

The CNS and PNS allow the body to interact and respond to the environment, ensuring we can function optimally in a complex network of sensory inputs, integrative processes, and command outputs.

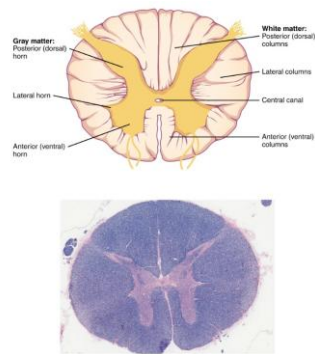


Figure 1.6: Grey and White Matter of the Spinal Cord [14]

# Chapter 1: Summary

In this first chapter, you have embarked on the beginning of your journey to the world of neural engineering, beginning with an exploration of neurons, the



building blocks of the nervous system. We uncovered the diversity and complexity of neurons by discussing their morphology, functionality, and mechanisms for neural communication. Then, we explored synaptic transmission and the nervous system's organization to understand better the complexity underlying our every sensation, thought, and action. We have laid a solid foundation for your next journey in Chapter 2, exploring the Hodgkin-Huxley model. In this chapter, we will dive deeper into the principles governing neuron excitability, paving the way for understanding neural functioning and the development of innovative technologies aimed at interfacing the nervous system.

# Chapter 1: Learning activities

## Learning Activity 1.1

### *Exploring Action Potentials Through Simulations*



#### *Objective*

To understand the characteristics and dynamics of action potentials by comparing different online simulations.

#### *Materials Needed*

- Computers or tablets with internet access
- Projector or whiteboard for class discussion
- Notebooks or digital note-taking tools

#### *Instruction:*

##### **Step 1: Individual Exploration**

Find and explore an online simulation of an action potential. Some popular options might include:

- The "NeuroLab Action Potential Simulator" by the University of Utah
- "Interactive Neuron Model" on the HHMI Biointeractive website
- "Action Potential Simulator" on PhET Interactive Simulations

Spend about 15-20 minutes interacting with the simulation. Take notes on the key features, such as the action potential phases (depolarization, repolarization, hyperpolarization), the role of ion channels, and the overall shape of the action potential graph.

##### **Step 2: Group Discussion**

Pair up with another student and share your findings. Discuss the following:

- **Commonalities:** What similarities did you notice between the two simulations? Consider aspects like the basic shape of the action potential, the phases (depolarization, repolarization, hyperpolarization), and the role of ion channels.

- **Differences:** What differences did you observe? Consider variations in the simulation interface, the level of detail provided, and any differences in how ion channel activity is depicted.

Discuss and make note of the explanations provided by each simulation for the phenomena occurring during an action potential. For instance, how does each simulation explain the opening and closing of sodium and potassium channels?

### Step 3: Class Discussion

Reconvene as a class and present your findings. Each pair should address the following:

- Summarize the common aspects observed in the simulations.
- Highlight and explain the differences you found.
- Describe the phenomena of the action potential as observed in the simulations. Include explanations for:
  - **Depolarization:** How and why the membrane potential rises.
  - **Repolarization:** The process of returning to the resting membrane potential.
  - **Hyperpolarization:** Why the membrane potential temporarily becomes more negative than the resting potential.
  - **Ion Channel Activity:** The role of sodium and potassium channels in the action potential phases.
- Be prepared to discuss any questions or clarifications that arise from the class discussion.

### Debrief:

- Conclude with a summary of key points learned from the activity.
  - Reflect on how simulations can aid in understanding complex biological processes like action potentials.
  - Discuss any insights gained about the similarities and differences between different simulation tools.
-

## Learning Activity 1.2

### ***Buzz groups: Block diagram of the nervous system 10min***



Buzz groups are a collaborative learning strategy used in educational and training settings to facilitate discussion and idea generation among participants. The technique involves dividing a large group into smaller subgroups, typically consisting of 4 to 6 members, who then engage in focused discussions on a specific topic or question for a short period of time, usually around 10-15 minutes. The name "buzz groups" comes from the lively and energetic nature of these small-group discussions, which can often sound like a buzzing noise when many groups talk simultaneously.

#### ***Key Features of Buzz Groups:***

- **Small Size:** Each buzz group is kept small to ensure that every member has an opportunity to contribute to the discussion.
- **Focused Discussion:** Groups are given a specific question or topic to discuss, which helps to keep the conversation on track and productive.
- **Time-Limited:** Discussions are typically short, creating a sense of urgency and encouraging participants to share their ideas quickly and concisely.
- **Reporting Back:** After the discussion, each buzz group usually reports their findings, ideas, or questions back to the larger group, facilitating a broader exchange of ideas.
- **Facilitation:** An instructor or facilitator may guide the process by providing the discussion topic, setting the time limit, and helping to synthesize and integrate the groups' findings.

#### ***Benefits of Buzz Groups:***

- **Increased Participation:** By breaking a large group into smaller units, more participants will likely speak up and engage in the discussion.
- **Diverse Perspectives:** Buzz groups allow for a variety of viewpoints to be expressed and considered, leading to richer and more comprehensive discussions.

- **Active Learning:** Participants are actively involved in the learning process, which can enhance understanding and retention of the material.
- **Critical Thinking:** The format encourages participants to think critically and creatively while discussing and analyzing the topic.
- **Collaboration Skills:** Working in small groups helps participants develop and practice collaboration and communication skills.

Phase 1: Create random groups of 2-3 people. Propose the following question. Draw a block diagram describing the functional behavior of the nervous system. Give 10 to 15 min, encourage students not to look at internet resources initially and to try to reason their diagram.

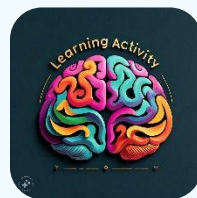
Phase 2: report the block diagram to the rest of the class and share.

Inclusivity aspect of the class learning activity:

- **Collaboration:** tasks are given in teams, and technical discussions are expected.
  - **Representation:** Encourage the groups to integrate all members into the team. For example, everybody should hold a pen and draw the diagram at approximately the same time. When discussing the topic, all students should have approximately the same time to talk; in other words, everybody is heard and respected.
  - **Autonomy:** students get to pick the type of block diagram, which engineering aspects of the nervous system they want to be represented, etc.
  - **Safe space:** this activity is not graded. Through classroom discussion, students will be helped to complement their diagrams.
-

# Learning Activity 1.3

## *Understanding Action Potentials Through Interactive Gameplay*



### ***Objective***

To deepen understanding of the action potential process by playing an interactive game and discussing its various components and challenges.

### ***Materials Needed***

- Computers or tablets with internet access
- Access to the game: Action Potential in Neuron Game
- Notebooks or digital note-taking tools

### ***Instructions***

#### **Step 1: Individual Gameplay**

- Access the "Action Potential in Neuron" game using the provided link.
- Play the game individually to familiarize yourself with its mechanics and objectives.
- Take note of your scores and the time it took to complete the game.
- Record any aspects of the game that you found particularly challenging or confusing, especially in relation to the action potential process.

#### **Step 2: Group Discussion**

Form small groups of 3-4 students and share your individual experiences with the game.

- **Scores and Timing:** Briefly report your scores and completion times to each other. Discuss if there were any noticeable differences among group members.
- **Problematic Aspects:** Identify and discuss which parts of the game were the most challenging. Focus on specific aspects of the action potential that you found difficult to understand or replicate in the game.
- **Understanding the Action Potential:** Reflect on how the game represented different phases of the action potential, such as depolarization, repolarization, and hyperpolarization. Discuss whether the game effectively illustrated these concepts.

- **Need for Clarification:** Highlight any aspects of the action potential that need further explanation or were unclear in the game. Consider whether the game provided adequate information about ion channels, membrane potential changes, or other key elements.

### Step 3: Class Discussion

Reconvene as a class and share your group's findings.

- **Common Challenges:** Summarize the common difficulties faced by different groups. Discuss why certain aspects of the game were challenging and how they relate to the action potential process.
- **Game Effectiveness:** Evaluate the game's effectiveness in teaching the concepts of action potentials. Were there any elements of the game that were particularly helpful or misleading?
- **Further Explanation:** Based on the group discussions, identify any parts of the action potential process that need additional clarification. Be prepared to explain these concepts using diagrams or additional resources if needed.

### Debrief:

- Summarize the key takeaways from the activity, emphasizing the insights gained from both playing the game and discussing its content.
- Reflect on how interactive tools like games can enhance understanding of complex biological processes and where they might fall short.
- Discuss strategies for using similar interactive tools to improve learning in other areas of biology or science.



# Chapter 1: Lab introduction

In this series of lab exercises, you will explore the fundamental principles of neuroscience through practical applications using advanced engineering tools. These labs are designed to provide hands-on experience with MATLAB and Arduino, enabling you to deepen your understanding of neuron function, morphology, and simulation. You will begin by studying the structure and communication mechanisms of neurons, the brain's fundamental building blocks.

Using MATLAB and the TREES Toolbox, you will visualize and analyze the morphology of different neurons. This toolbox allows for comprehensive analysis and visualization of neuron structures, providing insights into how their shapes and forms influence their functions. By working with the provided datasets, you will generate visualizations to explore and compare the morphological differences between various neuron types.

In the subsequent lab, you will simulate the behavior of synthetic neurons using an Arduino microcontroller. This simulation will be based on the Hodgkin-Huxley model, a foundational mathematical model that describes how action potentials in neurons are generated and propagated through the movement of ions across the cell membrane. Throughout these labs, you will apply theoretical knowledge to practical scenarios, preparing you for further studies in neuroscience, biomedical engineering, and related fields.



# Chapter 1: Lab Example 1



## *Introduction*

This first chapter explains the fundamental principles of the brain, including the neurons, and how they communicate with one another to execute various functions throughout the body. We will apply what we have discussed to a practical engineering tool. In this first lab example, we will use MATLAB. This platform will provide the tools for simulating and analyzing the differences in morphology of different neurons using the TREES Toolbox. This toolbox is comprehensively designed to analyze and visualize neuron morphology structures. In this lab example, we will download the toolbox and generate visuals using the dataset provided to look at the morphology of different neurons.

## *Steps*

First, you will need to download MATLAB if you do not already have it; it will become useful in the neural engineering journey in this textbook and in many other instances of your engineering journey. Follow this link to download MATLAB

<https://www.mathworks.com/products/matlab/student.html>

After downloading MATLAB to your device, download the TREES toolbox using this link.

<https://www.mathworks.com/matlabcentral/fileexchange/68886-trees-toolbox>

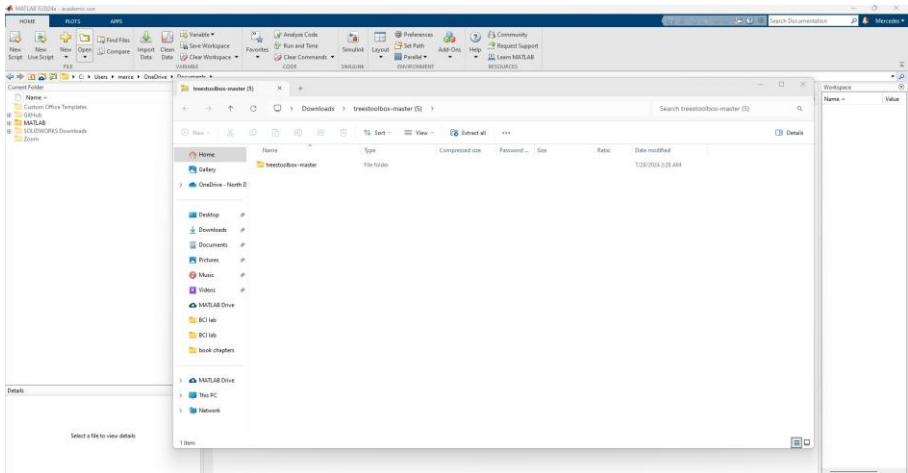


Figure 1.7: Pop up box

Once on the website, you will download the current version of the TREES toolbox from GitHub. The toolbox comes in the form of a zip file (Fig 1.7). When the zip file is downloaded onto your device, unzip the toolbox. Other toolboxes recommended for the TREES Toolbox are the Image Processing Toolbox, in polyhedron, and the Statistics and Machine Learning Toolbox, which can be added using the MATLAB Add-On Explorer. Now that we have the toolbox, we can explore it in MATLAB. The first step is to unzip the TREES toolbox file and then add the TREES Toolbox to your

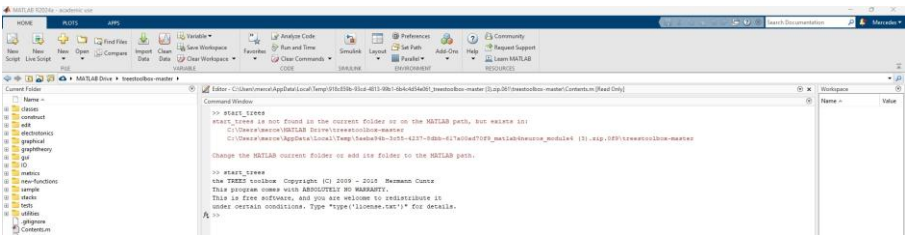


Figure 1.8: Red error message and successful upload message

MATLAB path. You do this by importing the file using the import folder button. Then right-click the file in the Current Folder box and select Add to Path. Once in your MATLAB path, code in `>>start_trees` in the command window. Another way to start the toolbox is by navigating to the `start_trees.m` file and clicking run. You will get the red error message if you have unsuccessfully uploaded the trees toolbox (Fig. 1.8). You will see the second message in black if you have successfully uploaded it.

Now that the toolbox is loaded into your MATLAB, we will visualize neuron morphology.

First, go to the command window and code `>>load_tree`. Once you have done that, MATLAB will open the Pick a file pop-up box (Fig. 1.9). Navigate to the samples folder, then to the mtr folder. The TREES toolbox saves the morphology files in .mtr format. We will select the sample .mtr file for this lab and click Open.

Next, to upload the sample as a visual image, code `>>fix_tree_UI` in the command window. You will be prompted with a pop-up box asking you to upload an input tree to be repaired. Click OK and navigate back to the “sample.mtr” file. You will then be prompted to upload a reference tree and navigate to the same “sample.mtr” file. Once you have uploaded the input and reference tree, a “fix\_tree\_UI” pop-up window will open, showcasing the sample.

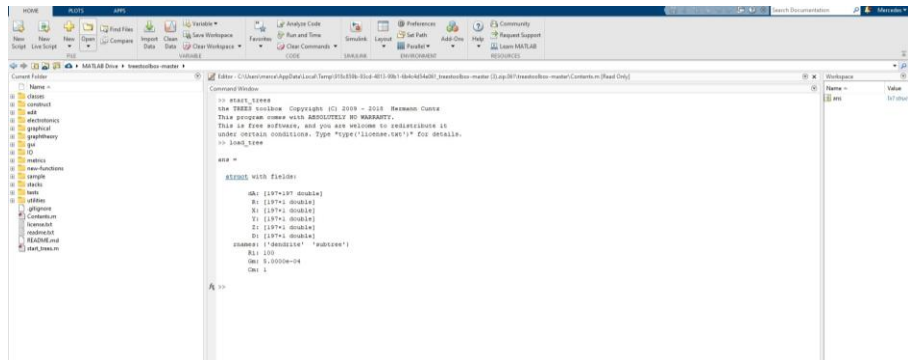


Figure 1.9: Results of `>>load_trees` command

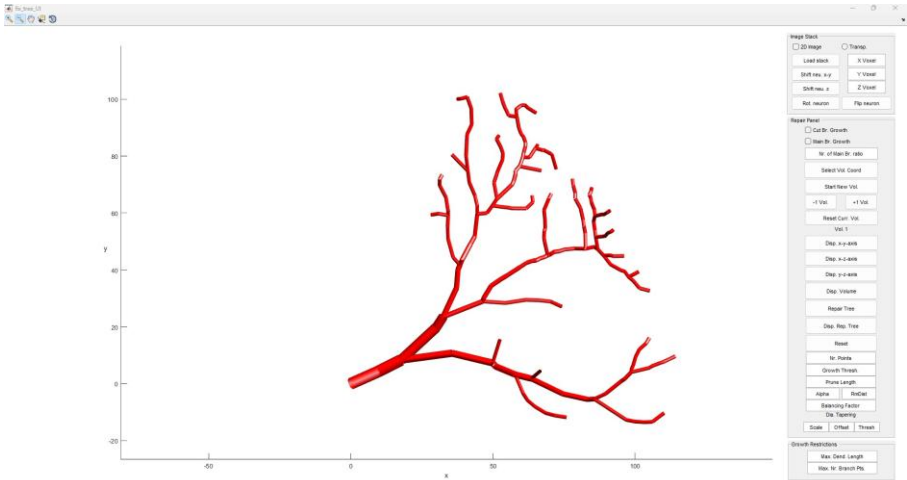


Figure 1.10: Trees upload result

Can you use your knowledge from this chapter to know what morphological structure is depicted in Fig. 1.10? If you said axon terminals, you are correct! In this sample, we see a visual representation of the axon terminals and a potential number of synaptic connections this sample could make.

Now, we will upload a new sample. Follow the same steps for the “sample.mtr” file, but choose the “hss.mtr” file instead. Remember to upload this as your tree to be repaired and your reference tree.

This file shows an example of an entire neuron showcasing all the morphological features (Fig. 1.11). You can use the zoom-in and zoom-out buttons in the top left corner to take a closer look at the different parts of the neuron. We can take this image rendering one step further by uploading an image stack.

Navigate to the Load stack button in the right-hand corner. The “Pick a file” pop-up menu will open. Navigate to the test, stacks, and data folders, and click the available stack image.

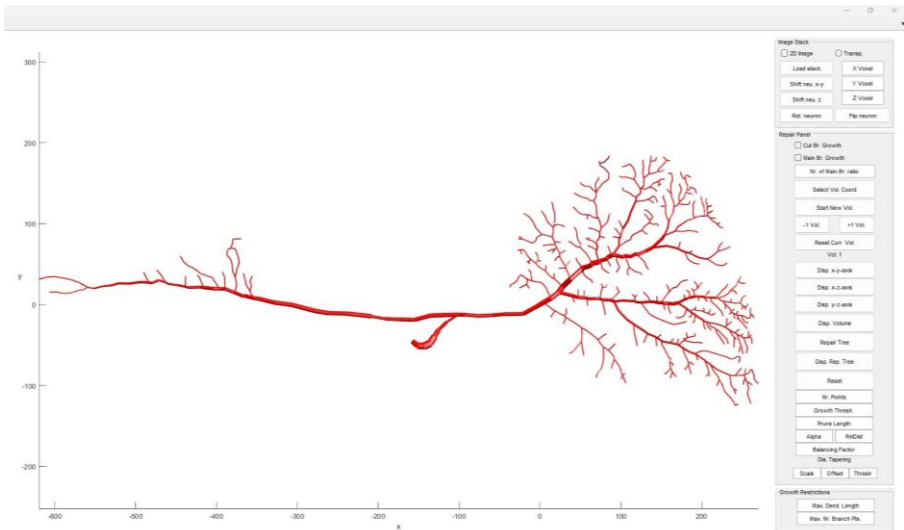


Figure 1.11: Visual of the entire neuron

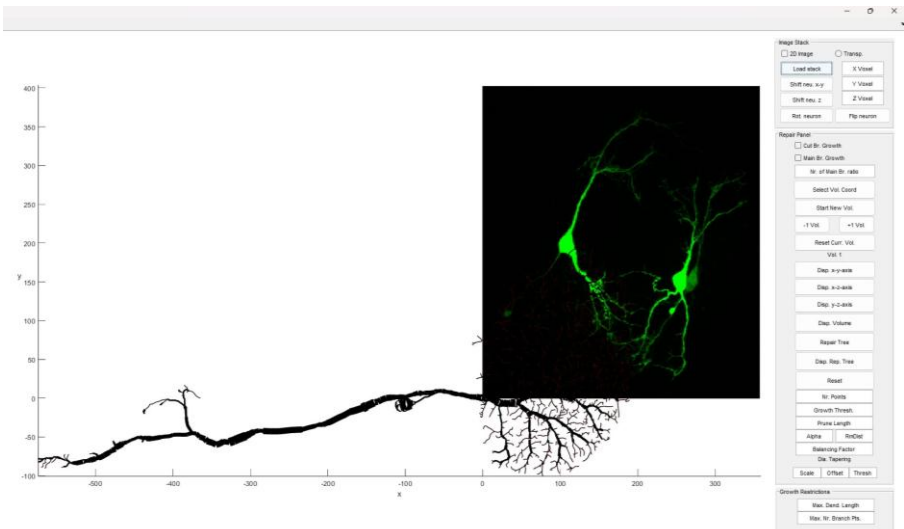


Figure 1.12: Entire neuron and its connections

In this new image rendering, we can see how the morphology of these neurons is situated and what other neurons around it look like (Fig. 1.12). This toolbox

can also visualize neurons, measure dendritic length, branch points, and surface area of neurons, and conduct statistical analysis on these parameters. We encourage you to continue exploring this toolbox to perform some of your analyses on the neuron samples provided.

### ***Other Examples and Resources***

Several other examples are available for you to use to keep exploring this toolbox. One resource type is Hermann Cuntz's free TREES toolbox tutorials on YouTube, which can be accessed using this link.

<https://www.youtube.com/@manodelcatan>

For more examples of practical applications of this chapter's content, please visit the book's dedicated GitHub repository page using this link.

[https://github.com/bddupre92/Neurobook\\_BME\\_UND](https://github.com/bddupre92/Neurobook_BME_UND)



## Chapter 1: Lab Example 2

## Synthetic Neuron Simulation with Arduino

This repository contains the code and instructions for simulating the behavior of a synthetic neuron using an Arduino microcontroller. The simulation is based on the Hodgkin-Huxley model, which describes how action potentials in neurons are initiated and propagated through the movement of ions across the cell membrane.



## Lab Overview

In this lab, you will:

1. Understand the Hodgkin-Huxley model and its application in simulating neuronal behavior.
2. Implement the Hodgkin-Huxley equations in Arduino code.
3. Simulate the behavior of a synthetic neuron and observe the output.
4. Use an oscilloscope to visualize the membrane potential signal.

### Materials Needed

- Arduino microcontroller
- Breadboard and connecting wires
- Resistors and LEDs (optional for visual representation of the output)
- Computer with Arduino IDE installed
- Oscilloscope

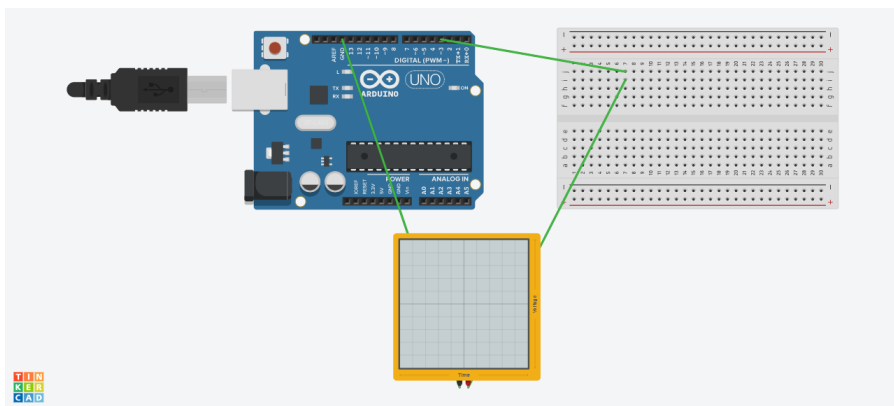


Figure 1.12: Initial hardware setup for the Arduino-based synthetic neuron

## ***Key Concepts***

### ***Hodgkin-Huxley Model***

The Hodgkin-Huxley model is a set of nonlinear differential equations that describe the ionic mechanisms underlying the initiation and propagation of action potentials in neurons. The model includes variables for membrane potential ( $V$ ) and gating variables ( $n$ ,  $m$ , and  $h$ ), representing the probability of open or closed ion channels.

- **Membrane Potential ( $V$ ):** The voltage difference across the neuron's membrane.
- **Gating Variables ( $n$ ,  $m$ ,  $h$ ):** Variables representing the state of potassium ( $n$ ), sodium activation ( $m$ ), and sodium inactivation ( $h$ ) gates.

### ***Equations***

The following vital equations define the model:

1. **Membrane Potential ( $V$ ):** Describes the change in membrane potential over time-based on ion conductance and injected current.
2. **Gating Variables ( $n$ ,  $m$ ,  $h$ ):** Describe the dynamics of the gating variables that affect ion channel conductance.

## ***Procedure***

### ***Setup the Arduino Environment***

1. Connect the Arduino to your computer.
2. Open the Arduino IDE and create a new sketch.

### ***Initialize Variables and Constants***

1. Define initial values for the gating variables ( $n1$ ,  $m1$ ,  $h1$ ) and membrane potential ( $V1$ ).
2. Define constants such as membrane capacitance ( $C$ ), maximum conductance for potassium ( $g_{k\_max}$ ), sodium ( $g_{Na\_max}$ ), and leak channels ( $g_L$ ), and equilibrium potentials for potassium ( $E_K$ ), sodium ( $E_{Na}$ ), and leak channels ( $E_L$ ).

### ***Implement the Hodgkin-Huxley Equations***

1. Write functions to calculate the derivatives of the gating variables (`n_prime`, `m_prime`, `h_prime`).
2. Update the state of the neuron in the `loop` function by calculating new values for the gating variables and membrane potential.

### ***Output the Membrane Potential***

1. Use the `analogWrite` function to output the membrane potential to pin 3 on the Arduino.
2. Connect pin 3 to the oscilloscope to visualize the signal.

### ***Connecting the Oscilloscope***

1. Connect the ground probe of the oscilloscope to the ground pin on the Arduino.
2. Connect the signal probe of the oscilloscope to pin 3 of the Arduino.
3. Turn on the oscilloscope and set it to the appropriate voltage and time scales to visualize the signal from the Arduino.

### ***Arduino Code***

```
// Synthetic Arduino neuron simulation

// Initial values for gating variables and membrane
potential
double n1 = 0.0003;
double m1 = 0.0011;
double h1 = 0.9998;
double V1 = -10;

// Constants for the neuron model
double C = 1;           // Membrane capacitance
double g_k_max = 36;    // Maximum conductance for
potassium channels
double g_Na_max = 120;  // Maximum conductance for
sodium channels
double g_L = 0.3;       // Conductance for leak
channels
```

```

double E_K = -12;           // Potassium equilibrium
potential
double E_Na = 115;          // Sodium equilibrium
potential
double E_L = 10.613;        // Leak equilibrium
potential
double d_t = 0.04;          // Time step for the
simulation
double I_inj = 10;          // Injected current

// Variables to store the current state of the neuron
double n, m, h, V;
double n_new, m_new, h_new, V_new;

void setup() {
    // Setup code to run once
    pinMode(3, OUTPUT);      // Set pin 3 as output
    Serial.begin(9600);      // Begin serial
communication at 9600 baud rate

    // Initialize the state variables
    n = n1;
    m = m1;
    h = h1;
    V = V1;
}

void loop() {
    // Main loop for the simulation

    // Calculate the derivatives of the gating variables
    double dn = n_prime(n, -V);
    double dm = m_prime(m, -V);
    double dh = h_prime(h, -V);

    // Update the gating variables
    n_new = n + dn * d_t;
    m_new = m + dm * d_t;
    h_new = h + dh * dt;

```

```

// Calculate the change in membrane potential
double dV = 1 / C * (-1 * g_k_max * pow(n, 4) * (V -
E_K)
                - g_Na_max * pow(m, 3) * h * (V -
E_Na)
                - g_L * (V - E_L) + I_inj);
V_new = V + dV * d_t;

// Output the updated membrane potential to pin 3
analogWrite(3, V_new + 20);

// Update the state variables for the next iteration
n = n_new;
m = m_new;
h = h_new;
V = V_new;
}

// Function to calculate the derivative of the n-gating
variable
double n_prime(double n, double V) {
    double k_1 = (0.01 * (V + 10)) / (exp((V + 10) / 10) -
1);
    double k_2 = 0.125 * exp(V / 80);
    double dn = k_1 - (k_1 + k_2) * n;
    return dn;
}

// Function to calculate the derivative of the m gating
variable
double m_prime(double m, double V) {
    double k_1 = 0.1 * (V + 25) / (exp((V + 25) / 10) -
1);
    double k_2 = 4 * exp(V / 18);
    double dm = k_1 - (k_1 + k_2) * m;
    return dm;
}

```

```
// Function to calculate the derivative of the h gating
variable
double h_prime(double h, double V) {
    double k_1 = 0.07 * exp(V / 20);
    double k_2 = 1 / (exp((V + 30) / 10) + 1);
    double dh = k_1 - (k_1 + k_2) * h;
    return dh;
}
```

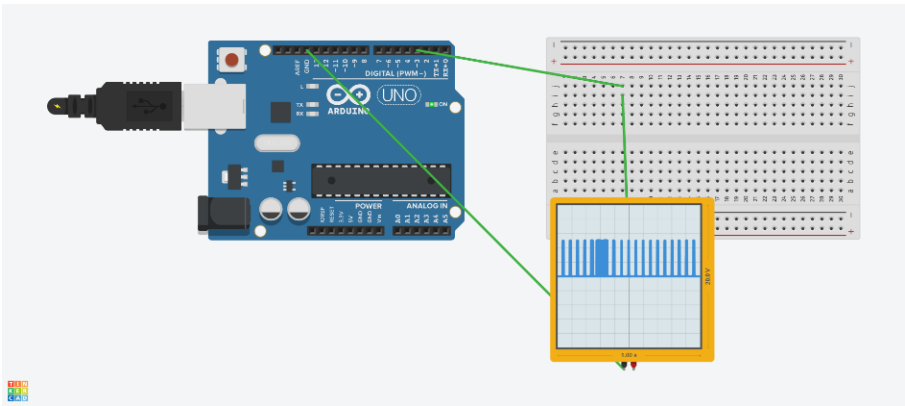


Figure 1.12: Arduino-based neuron firing

### ***Synthetic neuron extended: Neuron Simulation with Adjustable Threshold***

Another extension to this lab can be to adjust some of the variables reading the ADC from a potentiometer.

### ***Overview***

This extension of the previous lab enhances the synthetic neuron simulation lab by adding a potentiometer to adjust the action potential threshold dynamically. The simulation is based on the Hodgkin-Huxley model, which describes the initiation and propagation of action potentials in neurons.

## Objectives

1. Integrate a potentiometer into the Arduino setup.
2. Modify the code to read the potentiometer value and adjust the action potential threshold ( $I_{inj}$ ).
3. Using an oscilloscope, visualize the effects of changing the threshold on the membrane potential.

### ***Materials Needed***

- Arduino microcontroller
- Breadboard and connecting wires
- Potentiometer (10k $\Omega$  recommended)
- Resistors and LEDs (optional for visual representation of the output)
- Computer with Arduino IDE installed
- Oscilloscope

## Setup

## Connecting the Potentiometer

1. Connect one outer pin of the potentiometer to the 5V pin on the Arduino.

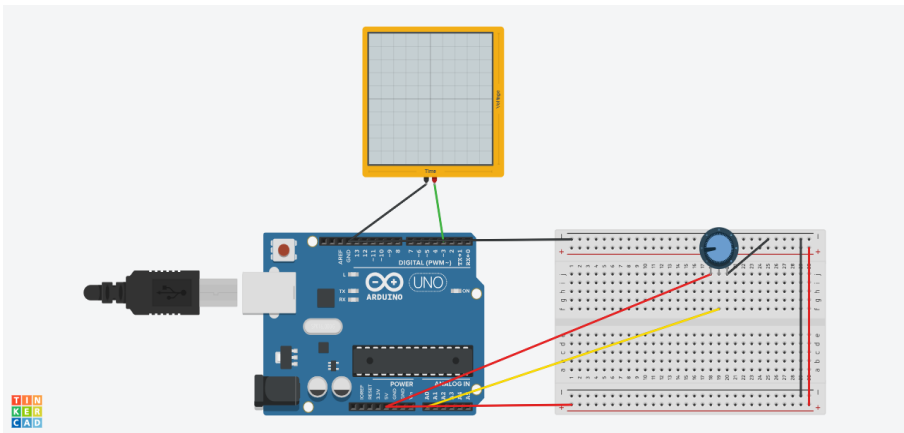


Figure 1.12: Initial hardware setup of Arduino with potentiometer

2. Connect the other outer pin to the GND pin.
3. Connect the middle pin (wiper) to an analog input pin on the Arduino (e.g., A0).

Arduino Code snippet

```
void loop() {  
  // Read the potentiometer value (0-1023)  
  int potValue = analogRead(A0);  
  
  // Map the potentiometer value to a suitable range for  
  I_inj (e.g., 0 to 20)  
  double I_inj = map(potValue, 0, 1023, 0, 20);  
}
```

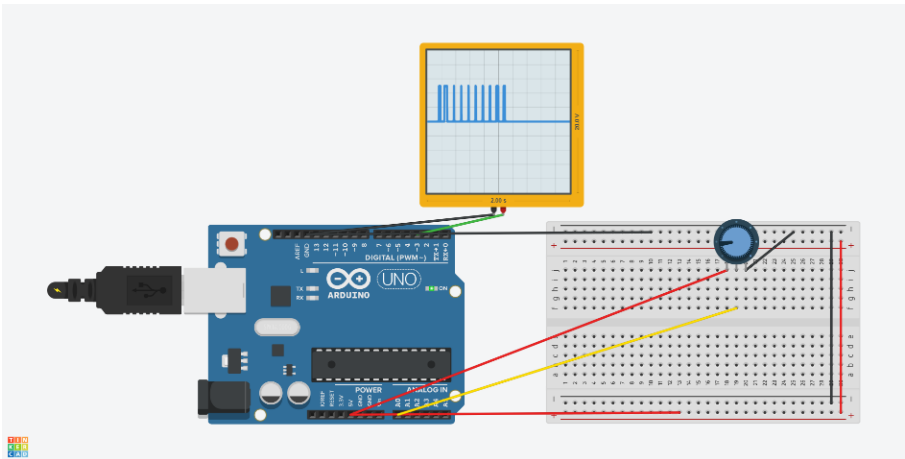
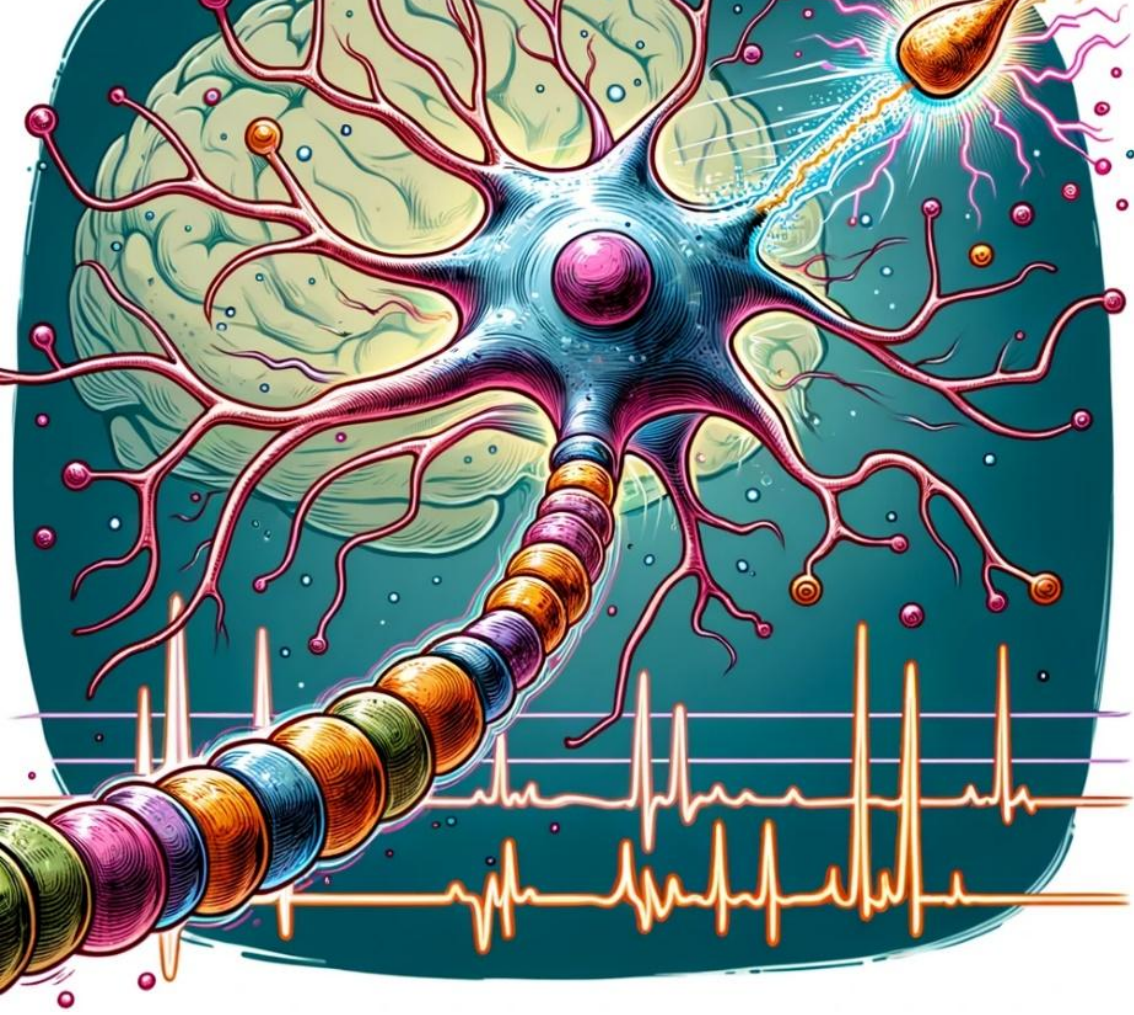


Figure 1.12: Arduino-based neuron firing







## Chapter 2

# Hodgkin-Huxley Model, Mathematical Modeling of Neurons

# Introduction and Learning Objectives

In this chapter, we will explore the critical role of the Hodgkin-Huxley model in neuroscience. This model has been fundamental in understanding how neurons generate and propagate electrical signals. The chapter will provide a comprehensive understanding of the historical impact, experimental setups, and broader applications of the Hodgkin-Huxley model. By the end of this chapter, you will be able to:

1. *Understand the historical impact of the Hodgkin-Huxley model and how it has revolutionized neuroscience.*
2. *Analyze the vital experimental setups and data that led to the development of the Hodgkin-Huxley model.*
3. *Learn how the Hodgkin-Huxley model can be generalized to understand diverse and complex neurons, including those in humans.*
4. *Recognize the transformative effects of the Hodgkin-Huxley model on neuroscience research and applications.*
5. *Demonstrate knowledge of the experimental techniques and data underpinning the development of the Hodgkin-Huxley model.*
6. *Apply the principles of the Hodgkin-Huxley model to various types of neurons and understand its broader implications in neuroscience.*

## Historical Context

The Hodgkin-Huxley model has been crucial in advancing our understanding of neuronal behavior. By modeling the ionic mechanisms underlying the action potential, this model has provided insights into the functioning of neurons and laid the foundation for numerous advancements in neuroscience. Understanding the historical development, foundational experiments, and broad applications of the Hodgkin-Huxley model will equip you with a deeper appreciation of its significance and versatility.

# Early Neuroscience: Foundations and Challenges



Figure 2.1: Ramon y Cajal in 1899 [15]

Neuroscience as a distinct scientific field began in the late 19th and early 20th centuries. This period saw significant advances in our understanding of the nervous system, primarily driven by technological innovations and groundbreaking theoretical work. Despite these advances, the mechanisms underlying neuronal signaling remained largely mysterious.

One of the earliest figures to leave a mark on the field was Santiago Ramón y Cajal (Fig. 2.1 [15]), often called the father of modern neuroscience. Cajal's

studies of neural tissues using the Golgi staining method provided detailed insights into the structure of neurons. His work demonstrated that neurons are more discrete entities than a continuous network, which was previously believed under the reticular theory. This discovery laid the groundwork for the neuron doctrine, which states that the neuron is the fundamental unit of the nervous system [16].

Camillo Golgi, whose staining technique made Cajal's discoveries possible, also contributed significantly to early neuroscience (Fig 2.2 [17]). Although Golgi initially supported the reticular theory, his invention of the silver nitrate staining method allowed for



Figure 2.2: Camillo Golgi in his lab [17]

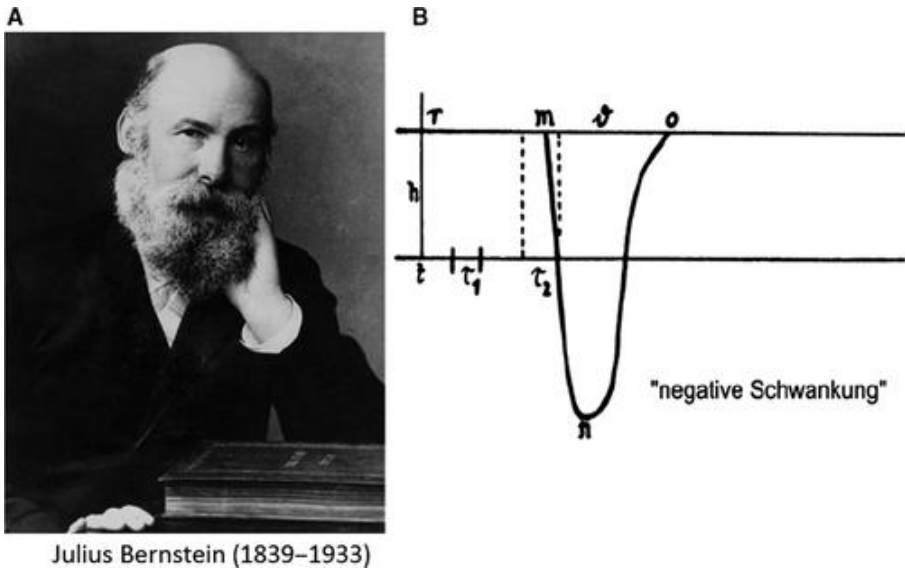


Figure 2.3: Bernstein and membrane theory permission pending [22]

unprecedented visualization of neuronal structures. This technique, known as the Golgi stain, remains a pivotal tool in neuroanatomy [18],

### *Additional Historical Figures*

- **Charles Sherrington:** His work on synapses and reflexes provided crucial insights into neuronal communication and integration [19].
- **Edgar Adrian:** Known for his work on the electrical activity of neurons, Adrian's discoveries about nerve impulses contributed to our understanding of how information is transmitted in the nervous system [20].

Despite these structural insights, neurons' electrophysiological properties were poorly understood. Early 20th-century neuroscientists faced substantial technical limitations. The tools available at the time, such as rudimentary electrodes and recording devices, were insufficient for detailed electrophysiological studies. Researchers could observe gross electrical

activity in the brain but lacked the precision to dissect the ionic mechanisms at play within individual neurons [21].

### ***Theoretical Beginnings: Membrane Theory***

In the late 19th century, Julius Bernstein proposed the first significant theory regarding the electrical properties of neurons, known as the "membrane theory" (Fig. 2.3 [22]). Bernstein suggested that neurons generate electrical signals through changes in membrane permeability to ions. He postulated that the resting membrane potential of a neuron resulted from the differential distribution of ions across the cell membrane, with a higher concentration of potassium ions ( $K^+$ ) inside the cell and a higher concentration of sodium ions ( $Na^+$ ) outside [18].

While Bernstein's membrane theory was a crucial step forward, it lacked empirical support and detailed explanation. The theory did not account for the dynamic action potential generation and propagation processes. Moreover, the experimental techniques of the time were not advanced enough to test Bernstein's hypotheses rigorously.

### ***Technological Advances: Cathode Ray Oscilloscope***

The early 20th century saw the development of new technologies that would eventually enable more precise electrophysiological studies. One such advancement was Karl Ferdinand Braun's invention of the cathode ray oscilloscope. This device allowed for the visualization of electrical signals and gave researchers a powerful tool to study neuronal activity. The oscilloscope could display rapid changes in voltage, making it possible to observe the electrical behavior of neurons in real-time [20].

The oscilloscope, along with other technological innovations such as improved amplifiers and recording equipment, paved the way for more detailed investigations into the electrical properties of neurons. These tools were essential for the subsequent work of Hodgkin and Huxley, who would bring a new level of precision to studying neuronal electrophysiology [21].

## ***Other Early Experiments and Observations***

Before Hodgkin and Huxley's work, other researchers had significantly contributed to understanding neuronal electrical activity. Keith Lucas, a British physiologist, conducted early experiments on the electrical properties of nerve fibers. Lucas's work on the conduction velocity of nerve impulses provided essential insights into the speed at which electrical signals travel along neurons. Although his studies were limited by the technology of the time, they laid the groundwork for future research.

In the 1930s, Kenneth Cole developed the voltage clamp technique, which allowed researchers to control the membrane potential of a neuron and measure the resulting ionic currents. This breakthrough technique enabled precise ionic current measurements, contributing to action potential generation. Cole's work on the electrical properties of cell membranes was instrumental in developing the Hodgkin-Huxley model [23].

## **The Hodgkin-Huxley Model**

### ***Alan Hodgkin and Andrew Huxley's Pioneering Work***

In the early 1950s, Alan Hodgkin and Andrew Huxley (Fig. 2.4 [24]) embarked on a series of groundbreaking experiments that would fundamentally alter our understanding of how neurons generate and propagate electrical signals. Their work focused on the squid's giant axon, an experimental model chosen for its large size, facilitating precise electrophysiological measurements [25]. The insights gained from these experiments led to the Hodgkin-Huxley model, a set of mathematical equations that describe the ionic mechanisms

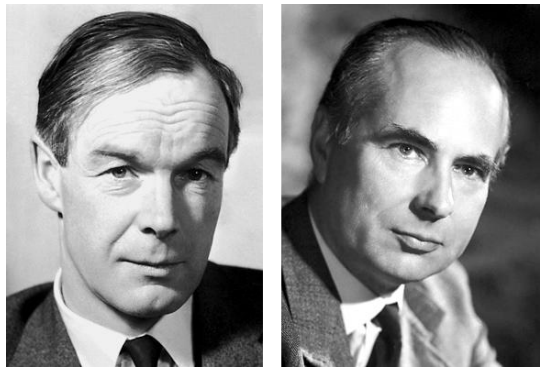


Figure 2.4: Hodgkin and Huxley [24]

underlying action potentials. The choice of the squid's giant axon as an experimental model was pivotal in advancing our understanding of neuronal function. The squid's giant axon, which can be up to 1 mm in diameter, provided a unique opportunity for detailed electrophysiological studies. Its large size made it easier to insert electrodes and precisely measure electrical activity. This feature was crucial for the experiments conducted by Hodgkin and Huxley, as it allowed them to perform detailed analyses that were impossible with smaller mammalian neurons [21]. One of the key technological advancements that enabled Hodgkin and Huxley's discoveries was Kenneth Cole's development of the voltage clamp technique in the 1930s. The voltage clamp allowed researchers to control the membrane potential of a neuron while measuring the ionic currents that flowed across the membrane [21]. This revolutionary technique separated the voltage control from the current measurement, providing a clear view of the ionic processes occurring during an action potential.

### ***Experimental Procedure and Key Findings***

Hodgkin and Huxley conducted their experiments by isolating the squid's giant axon and inserting electrodes to apply voltage clamps (Fig. 2.5 [26]).

They varied the membrane potential and recorded the resulting ionic currents. Through these experiments, they discovered two main ionic currents responsible for the action potential: a rapidly activating inward current carried by sodium ions ( $\text{Na}^+$ ) and a more slowly activating outward current carried by potassium ions ( $\text{K}^+$ ) [25].

## *Mathematical Modeling*

Hodgkin and Huxley went beyond merely describing their experimental observations; they developed a set of mathematical equations that quantitatively described the ionic mechanisms underlying action potentials. Understanding that conductance (denoted as  $g$ ) represents the ease with which ions can flow through channels in the neuron's membrane is essential. Conductance depends on the number and state of ion channels open at any given time and can vary dynamically during the action potential. The model explicitly addresses the conductance of potassium ( $g_K$ ) and sodium ( $g_{Na}$ ) ions,

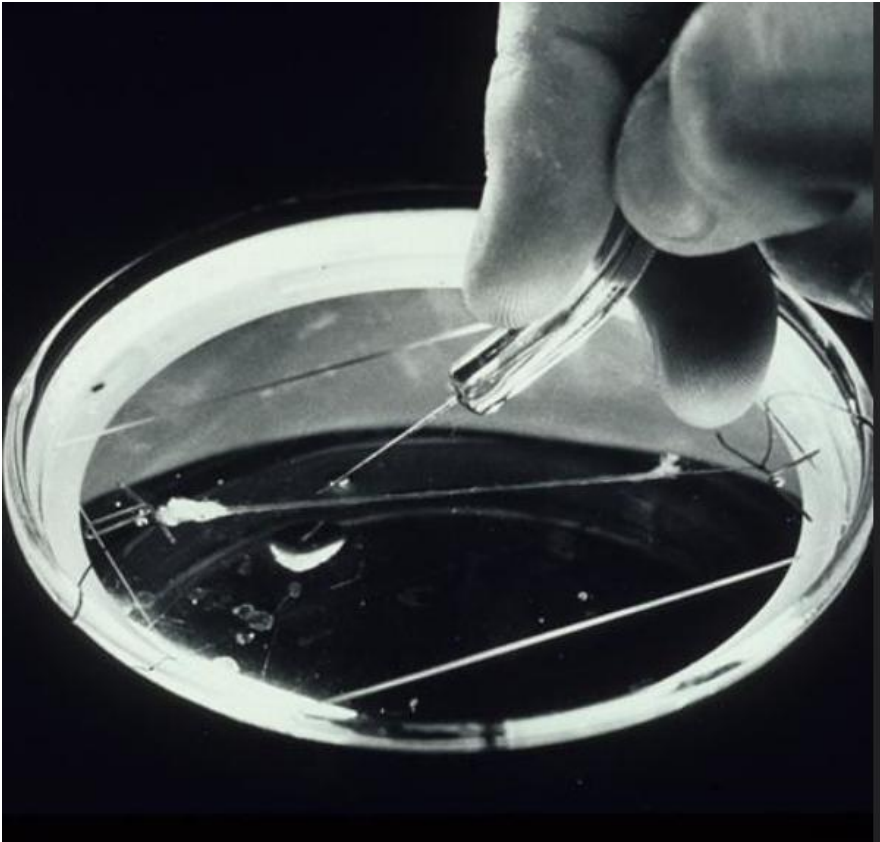


Figure 2.5: Dissection of the Giant Squid Axon [26]

which play crucial roles in the generation and propagation of action potentials [23]. Their model included several vital components, also shown in Fig. 2.7 [27]:

- Sodium Conductance( $g_{Na}$ ): Describes the flow of sodium ions into the neuron, which is responsible for the initial rapid depolarization phase of the action potential.
- Potassium Conductance ( $g_K$ ): Describes the flow of potassium ions out of the neuron, which is responsible for the repolarization phase that follows the peak of the action potential.
- Leakage Conductance ( $g_L$ ): Accounts for the small, steady flow of ions not carried by voltage-gated channels, contributing to the resting membrane potential.
- Membrane Capacitance ( $C_m$ ): Represents the ability of the neuron's membrane to store and separate charge [28].

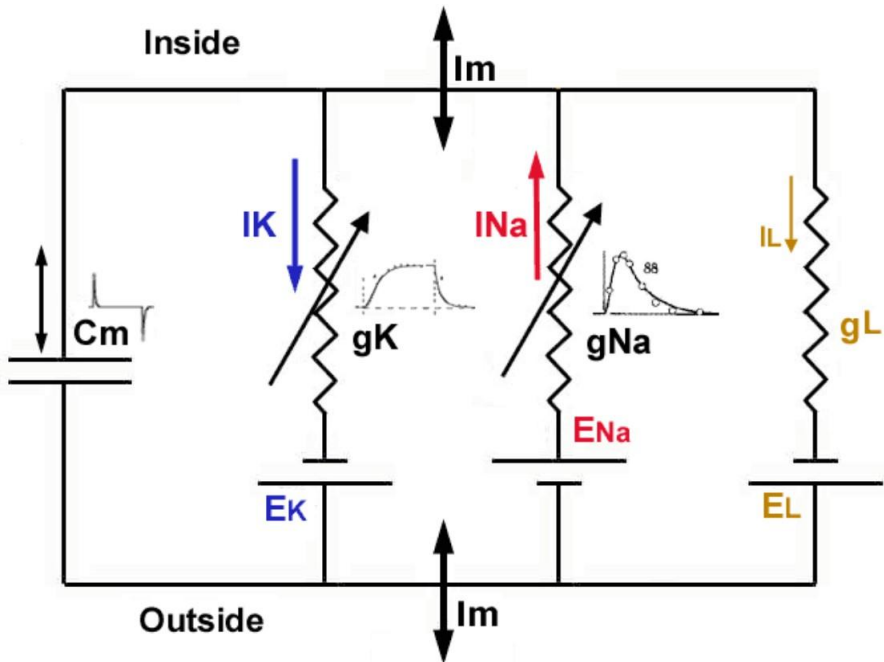


Figure 2.6: Hodgkin & Huxley Model Circuit Representation [27]

The core of the Hodgkin-Huxley model is expressed through a set of differential equations that describe how these conductances change over time and in response to changes in membrane potential. These equations provided a comprehensive framework for understanding the dynamics of action potential generation and propagation.

$$\frac{dV}{dt} = \frac{1}{C_m} (I_{Na} + I_K + I_L + I_{ext}) \quad (2.1)$$

Where:

- $V$  is the membrane potential.
- $I_{Na}$ ,  $I_K$ , and  $I_L$  are the sodium, potassium, and leakage currents, respectively.
- $I_{ext}$  is the externally applied current.
- $C_m$  is the membrane capacitance.

The model also included equations for the gating variables  $m$ ,  $h$ , and  $n$ , which describe the probability of ion channels being open or closed:

$$\frac{dm}{dt} = \alpha_m(1 - m) - \beta_m m \quad (2.2)$$

$$\frac{dh}{dt} = \alpha_h(1 - h) - \beta_h h \quad (2.3)$$

$$\frac{dn}{dt} = \alpha_n(1 - n) - \beta_n n \quad (2.4)$$

Where  $\alpha$  and  $\beta$  are voltage-dependent rate constants.

***Revolutionizing Neuroscience***

The Hodgkin-Huxley model was revolutionary for several reasons. First, it provided a quantitative description of the ionic basis of action potentials, allowing for precise predictions of neuronal behavior under various conditions. Second, it demonstrated the power of combining experimental data with mathematical modeling, setting a new standard for research in biophysics and neurophysiology [19].

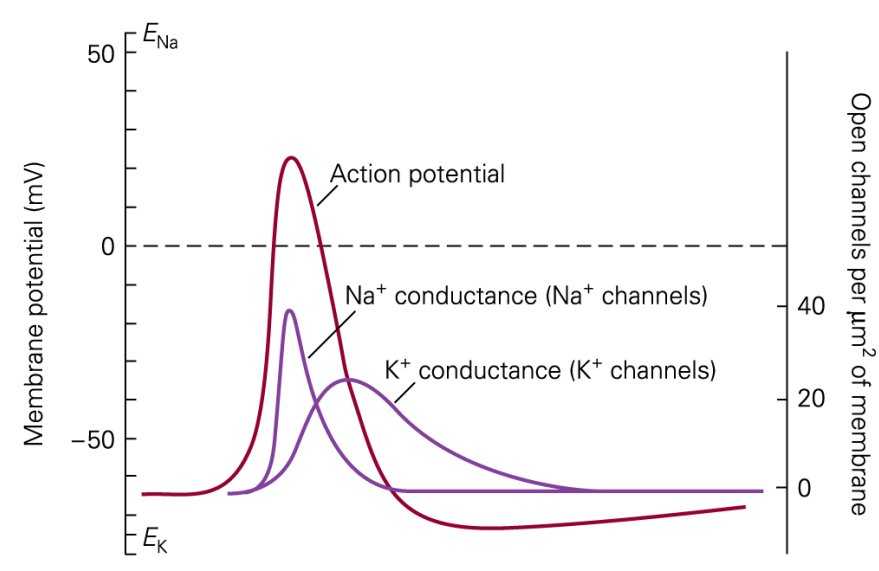


Figure 2.7: Hodgkin & Huxley model Representation [27]

The publication of Hodgkin and Huxley's findings in a series of landmark papers in 1952 profoundly impacted the field of neuroscience. Their work explained how action potentials are generated and provided a framework that could be applied to other types of neurons and excitable cells. The Hodgkin-

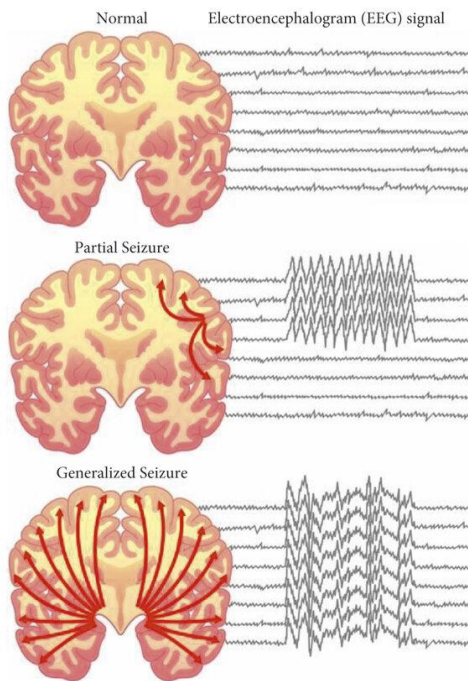


Figure 2.8: Healthy Brain Vs Brain with Seizures [29]

Huxley model became a foundational tool in electrophysiology and computational neuroscience, influencing various research areas [21].

## Applications and Extensions of the Model

The Hodgkin-Huxley model has been widely applied and extended since its original formulation. Researchers have used the model to study various aspects of neuronal function, including:

- **Neural Coding:** Investigating how neurons encode and transmit information through patterns of action potentials.
- **Neural Plasticity:** Exploring how changes in ion channel properties can affect synaptic plasticity and learning.
- **Disease Mechanisms:** Understanding the ionic basis of neurological disorders such as epilepsy, where abnormal ion channel function leads to excessive neuronal excitability.
- **Pharmacology:** Testing the effects of drugs on ion channel behavior and neuronal excitability, aiding in the development of new treatments for neurological conditions.

Extensions of the Hodgkin-Huxley model have incorporated additional complexities, such as the role of calcium ions ( $\text{Ca}^{2+}$ ) in neuronal signaling, the effects of temperature on ion channel kinetics, and the integration of synaptic inputs from other neurons.

For practical applications of this model, the studies below have utilized it in research on EEG, Epilepsy, and Behavioral Sciences (Fig 2.8 [29]).

1. A Computational Model to Determine Membrane Ionic Conductance Using Electroencephalography in Epilepsy
2. The Hodgkin-Huxley Heritage: From Channels to Circuits
3. Hodgkin and Huxley Opsin Model for Computationally Efficient Optogenetic Neurostimulation in Cells and Networks
4. Action Potential Initiation in the Hodgkin-Huxley Model

### ***Continuing Impact and Future Directions***

The Hodgkin-Huxley model remains a cornerstone of neuroscience research. Its principles continue to inform the development of new models and experimental techniques. Advances in computational power and high-throughput experimental methods have enabled the simulation of increasingly complex neural networks, building on the foundation of Hodgkin and Huxley. Future research aims to integrate the Hodgkin-Huxley model with new molecular biology and genetics insights, providing a more comprehensive understanding of neuronal function. For example, researchers are investigating

how genetic variations in ion channel genes contribute to individual differences in neuronal excitability and susceptibility to neurological diseases. The Hodgkin-Huxley model also serves as an educational tool, helping students and researchers grasp the fundamental principles of neuronal signaling. Its combination of experimental rigor and mathematical elegance inspires new generations of neuroscientists.

## The Hodgkin-Huxley Model's Lasting Influence

### Revolutionizing Neuroscience

The Hodgkin-Huxley model revolutionized neuroscience by providing a comprehensive and quantitative framework for understanding the electrical properties of neurons. Before their work, the mechanisms underlying action potentials were largely speculative, and the field lacked a unified theoretical foundation. The introduction of the Hodgkin-Huxley model marked a paradigm shift, transforming neuroscience into a more quantitative and predictive science [23].

The immediate impact of the Hodgkin-Huxley model was most strongly felt in the field of electrophysiology. By describing the ionic basis of action potentials, the model explained mechanistically the electrical signaling in neurons. This had several important implications:

- **Experimental Validation:** The Hodgkin-Huxley model offered a framework for designing and interpreting electrophysiological experiments. Researchers could now test specific predictions about ion channel behavior and neuronal responses to electrical stimuli.
- **Standardization of Techniques:** The success of the voltage clamp technique, which was crucial to Hodgkin and Huxley's discoveries, led to its widespread adoption. This technique became a standard method for studying ion channels and neuronal excitability, facilitating the replication and extension of their findings [21].
- **Advancement of Theory:** The mathematical rigor of the Hodgkin-Huxley model set a new standard for theoretical work in neuroscience.

It demonstrated the power of combining experimental data with mathematical modeling to understand biological processes better [19].

## **Foundational Role in Computational Neuroscience**

The Hodgkin-Huxley model is often considered the foundation of computational neuroscience, which uses mathematical models and computer simulations to study the nervous system. The model's equations describe how membrane potential changes are driven by ion channel dynamics, providing a basis for simulating neuronal behavior [23].

The Hodgkin-Huxley model enabled researchers to simulate the electrical activity of neurons and neural networks with unprecedented accuracy. These simulations have explored various aspects of neural function, including signal propagation, synaptic integration, and network dynamics.

The model has been instrumental in studying neural coding, which seeks understanding how neural circuits represent and process information. The Hodgkin-Huxley model has helped researchers investigate how neurons encode sensory inputs and generate motor outputs by describing action potential generation. The principles of the Hodgkin-Huxley model have influenced the development of artificial neural networks, which are used in machine learning and artificial intelligence [28] and will be discussed in Chapter 3. These networks, inspired by the structure and function of biological neurons, have been applied to a wide range of tasks, from image recognition to natural language processing.

## **Impact on Biomedical Research**

The Hodgkin-Huxley model has had significant implications for biomedical research, particularly in understanding and treating neurological disorders. By elucidating the ionic mechanisms underlying neuronal excitability, the model has provided insights into the pathophysiology of various conditions:

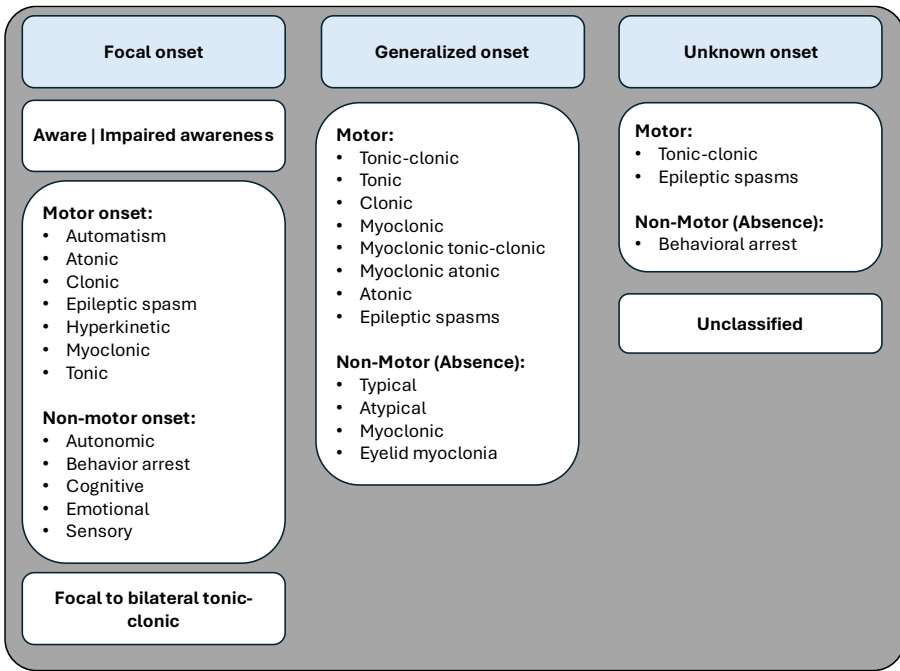


Figure 2.9: Seizures and brain activity [30]

- Epilepsy is characterized by abnormal, excessive neuronal activity (Fig. 2.9 [30]). The Hodgkin-Huxley model has been used to study the ionic basis of epileptic seizures, helping researchers identify potential targets for therapeutic intervention. For example, drugs that modulate sodium or potassium channels can help control seizure activity [21].
- Chronic pain is often associated with abnormal electrical activity in pain pathways. The Hodgkin-Huxley model has been used to investigate the role of ion channels in pain perception, leading to the development of drugs that target these channels to alleviate pain [28].

The principles of the Hodgkin-Huxley model have also been applied to cardiac electrophysiology. The model has helped researchers understand the ionic basis of cardiac action potentials and arrhythmias, contributing to developing treatments for heart rhythm disorders.

## ***Influence on Pharmacology***

The Hodgkin-Huxley model has been instrumental in pharmacology, where it is used to study drugs' effects on neuronal and cardiac function. The model provides a framework for predicting therapeutic and side effects by simulating drugs' impact on ion channels. The model is used in the early stages of drug development to screen potential compounds for their effects on ion channel function. This helps identify promising candidates for further testing and reduces the likelihood of adverse effects.

The Hodgkin-Huxley model provides mechanistic insights into how drugs interact with their targets. Researchers can optimize its efficacy and safety by understanding the specific ionic mechanisms a drug affects [21].

## ***Educational Value***

The Hodgkin-Huxley model is widely used as an educational tool in neuroscience and physiology courses. Its combination of experimental data and mathematical rigor provides an excellent example of how biological phenomena can be studied quantitatively.

The model teaches students about the electrical properties of neurons and the principles of electrophysiology. Its detailed, quantitative approach provides a clear framework for understanding complex biological processes. The mathematical basis of the Hodgkin-Huxley model allows for the creation of interactive simulations. These simulations enable students to visualize and manipulate the variables that influence neuronal behavior, enhancing their understanding of the underlying principles.

At the end of the chapter, we will delve into some example coding examples to understand further the Hodgkin-Huxley model and the use of an engineering tool for further learning and development.

## ***Broader Impact, Legacy, and Continuing Relevance***

The broader impact of the Hodgkin-Huxley model extends beyond neuroscience and medicine. Its principles have influenced a wide range of fields, demonstrating the interconnectedness of scientific disciplines. The success of the Hodgkin-Huxley model has inspired generations of researchers

to pursue similar integrative approaches. Scientists can better understand complex biological systems by combining experimental data with mathematical modeling. The model's influence extends to computer science, engineering, and physics. Its principles have been applied to developing new technologies and studying complex systems, highlighting the value of interdisciplinary collaboration.

The Hodgkin-Huxley model remains relevant today as ongoing research continues to build on its foundations. Advances in experimental techniques and computational power have enabled the development of more sophisticated models that incorporate additional complexities:

- New technologies, such as optogenetics and high-resolution imaging, provide detailed insights into neuronal function. These advancements complement the Hodgkin-Huxley model, allowing researchers to refine and extend its principles.
- Integrating the Hodgkin-Huxley model with molecular biology and genetics provides a more comprehensive understanding of neuronal function. For example, researchers are investigating how genetic variations in ion channel genes contribute to individual differences in neuronal excitability and susceptibility to neurological diseases.

The enduring impact of the Hodgkin-Huxley model underscores its importance as a foundational tool in neuroscience. Its combination of experimental rigor, mathematical elegance, and broad applicability continues to inspire discoveries and technological innovations.

## **Challenges and Limitations**

### ***Technological Advancements***

The Hodgkin-Huxley model, despite its revolutionary impact, was developed in an era with significant technological constraints. The tools and techniques available to Alan Hodgkin and Andrew Huxley were advanced for their time but limited compared to modern standards. Over the past several decades, technological advancements have addressed some of the limitations of the original model, enabling researchers to explore neuronal behavior in greater detail.

## ***High-Resolution Imaging***

High-resolution imaging is one of the significant advancements that has enhanced our understanding of neuronal function. Techniques such as two-photon and electron microscopy provide detailed images of neuronal structures at high spatial resolution. These imaging methods allow researchers to visualize the distribution and density of ion channels on the neuronal membrane, providing insights that were not possible with the tools available to Hodgkin and Huxley.

- Two-Photon Microscopy technique allows for the imaging of living tissue up to a millimeter deep, making it possible to study the activity of neurons in their natural environment. Two-photon microscopy has been used to observe calcium signaling in neurons, shedding light on the dynamics of ion channels and synaptic activity.
- Electron microscopy provides ultra-high-resolution images of neuronal structures, allowing researchers to visualize the detailed morphology of neurons and their connections. This technique has been instrumental in mapping the distribution of ion channels and understanding their role in neuronal function.

## ***Computational Power***

The increase in computational power has profoundly impacted the field of computational neuroscience. Modern computers can perform complex simulations that were unimaginable in Hodgkin and Huxley's time. This computational power allows for modeling entire neural networks, incorporating thousands or even millions of neurons, each with its own set of Hodgkin-Huxley equations. Advances in computational power have enabled the simulation of large-scale neural networks, providing insights into how individual neurons interact to produce complex behaviors. These simulations can incorporate detailed models of ion channel dynamics, synaptic interactions, and network connectivity.

Modern computational techniques allow for real-time simulations of neuronal activity, enabling researchers to study the immediate effects of changes in ion

channel properties or external stimuli. This capability is crucial for exploring dynamic processes such as learning, memory, and neural plasticity.

## ***Theoretical Developments***

While the original Hodgkin-Huxley model was a breakthrough, subsequent theoretical developments have expanded its scope and addressed some limitations. Researchers have developed new models incorporating additional complexities, providing a more comprehensive understanding of neuronal behavior.

The original Hodgkin-Huxley model primarily focused on sodium ( $\text{Na}^+$ ) and potassium ( $\text{K}^+$ ) channels. However, neurons possess a variety of other ion channels that play critical roles in their function. Subsequent models have incorporated these additional channels to provide a more accurate representation of neuronal dynamics:

- Calcium Channels ( $\text{Ca}^{2+}$ ) are essential for various neuronal processes, including neurotransmitter release and synaptic plasticity. Models incorporating calcium dynamics provide insights into the role of these channels in modulating neuronal excitability and signal transduction.
- Chloride Channels ( $\text{Cl}^-$ ) contribute to the inhibitory mechanisms in neurons. Including chloride dynamics in models helps explain the balance between excitation and inhibition in neural circuits.
- The original Hodgkin-Huxley model did not account for the complex, non-linear interactions between different types of ion channels. Modern models incorporate these interactions, providing a more realistic depiction of how ion channel activity shapes neuronal behavior.

The Hodgkin-Huxley model describes the behavior of a single, isolated neuron. However, neurons in the brain are part of complex networks and constantly receive inputs from other neurons. Modern models include synaptic inputs to simulate how neurons integrate information from their connections. Including excitatory and inhibitory synaptic inputs in models helps researchers understand how neurons process and respond to incoming signals. This

integration is crucial for studying neural coding, network dynamics, and information processing.

Synaptic plasticity, the ability of synapses to strengthen or weaken over time, is a fundamental mechanism underlying learning and memory. Models incorporating synaptic plasticity provide insights into how neural networks adapt and reorganize in response to experience.

### ***Alternative Models***

While the Hodgkin-Huxley model set a new standard, alternative models have been developed to address specific limitations and to simplify certain aspects for large-scale simulations.

The Fitzhugh-Nagumo model is a simplified version of the Hodgkin-Huxley model. It reduces the complexity of the equations while retaining the essential features of excitability and action potential generation. By reducing the number of variables and parameters, the Fitzhugh-Nagumo model makes it easier to study neurons' qualitative behavior and simulate large networks (Fig. 2.10 [31], [32]). This model is often used in theoretical studies to explore the dynamics of excitable systems and to analyze phenomena such as wave propagation and synchronization in neural networks [20].

The Morris-Lecar model incorporates additional biophysical details, such as the role of calcium channels, to accurately describe certain types of neurons. The Morris-Lecar model captures the behavior of neurons that rely heavily on calcium for their excitability and signaling by including calcium dynamics. This model is beneficial for comparing the dynamics of different types of neurons and for studying how variations in ion channel composition affect neuronal behavior [28].

### ***Challenges in Modeling Human Neurons***

Applying the Hodgkin-Huxley model to human neurons presents several challenges due to the complexity and diversity of human neural tissue. Human neurons exhibit a wide range of morphologies, ion channel types, and connectivity patterns that complicate the direct application of the original model.

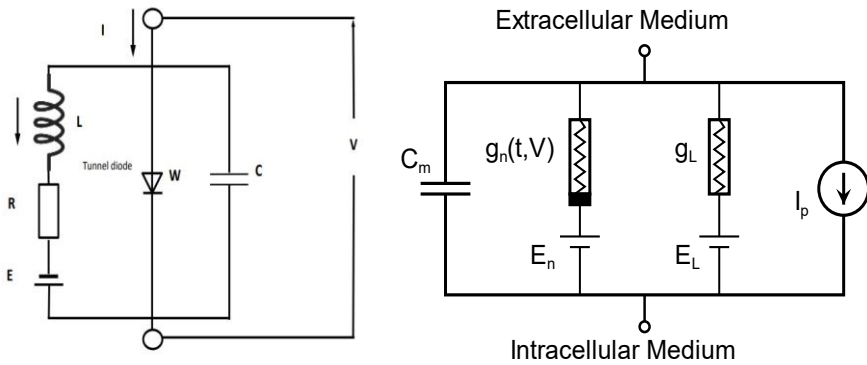


Figure 2.10: Fitzthugh-Nagumo circuit (left) and Hodgkin-Huxley circuit (right) [31], [32]

Human neurons have intricate structures with extensive branching dendrites and axons, which are not fully accounted for in the Hodgkin-Huxley model. This structural complexity influences how electrical signals are generated and propagated. Dendrites play a crucial role in integrating synaptic inputs. Models incorporating dendritic morphology and active properties accurately represent how neurons process information [18].

Axon myelination and branching affect the speed and fidelity of signal transmission. Including these factors in models helps explain the variability in conduction velocities and the mechanisms underlying action potential propagation.

Different types of neurons in the human brain serve distinct functions and exhibit unique electrophysiological properties. For example, excitatory neurons, which release neurotransmitters like glutamate, and inhibitory neurons, which release neurotransmitters like GABA, have different ion channel compositions and firing patterns.

- **Neuron Types:** Including the diversity of neuron types in models is essential for studying how different cells contribute to brain function. This involves characterizing each neuron type's specific ion channel properties and synaptic connections.

- **Network Interactions:** Understanding the interactions between different types of neurons in a network context is crucial for explaining complex behaviors such as sensory processing, motor control, and cognitive functions.

Advances in experimental techniques, such as patch-clamp recordings and high-throughput sequencing, provide detailed data on the properties of human neurons. These data-driven approaches are essential for refining and adapting the Hodgkin-Huxley model to human neural systems.

- Patch-clamp techniques allow for precisely measuring ionic currents in individual neurons. These recordings provide valuable ion channel kinetics and conductance data, which can be used to parameterize and validate models.
- High-throughput sequencing and other molecular techniques provide information on ion channel expression levels and genetic variants. Integrating this data into models helps explain individual differences in neuronal behavior and susceptibility to neurological disorders.

### ***Recent Advances in Theoretical Neuroscience***

Ongoing research in theoretical neuroscience aims to develop more comprehensive models that incorporate the complexities of human neurons and neural networks. These models build on the foundations laid by the Hodgkin-Huxley model and incorporate new insights from molecular biology, genetics, and advanced imaging techniques. Multi-scale models integrate information from different levels of organization, from molecular and cellular levels to the whole brain. These models bridge the gap between individual neurons' detailed properties and large-scale neural networks' more abstract behavior [23]. Fig. 2.11 [33] shows a Spiking Neural Network multi-scale model.

Modern models consider neurons' dynamic and non-linear behavior, such as voltage-gated ion channels, synaptic transmission, and plasticity. These dynamic systems approaches provide a deeper understanding of how neurons adapt and change over time in response to experience and environmental factors.

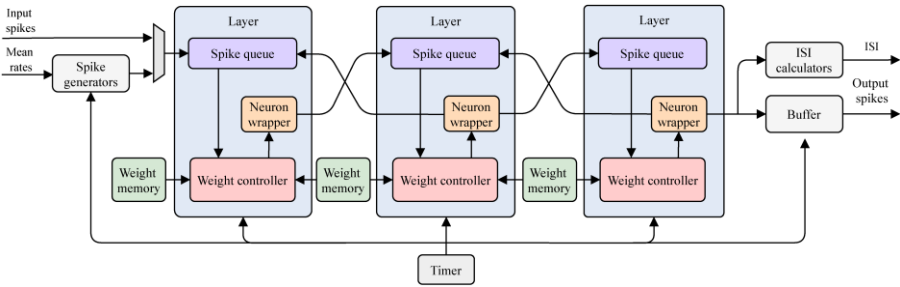


Figure 2.11: Compartmental Model for Multi Scale Models Spiking Neural Network [33]

## ***Future Directions and Emerging Technologies***

The field of neuroscience is rapidly evolving, with new technologies and theoretical developments continually pushing the boundaries of our understanding. Future research aims to refine and expand the Hodgkin-Huxley model, incorporating new data and addressing remaining challenges.

- Optogenetics allows for precise control of neuronal activity using light-sensitive proteins. This technology provides a powerful tool for testing model predictions and exploring the causal relationships between ion channel activity and neuronal behavior.
- Advances in high-throughput electrophysiology enable the simultaneous recording of electrical activity from large populations of neurons. This data can be used to validate and refine models, providing insights into the collective behavior of neural networks.
- Machine learning and artificial intelligence techniques are increasingly used to analyze complex neural data and develop predictive models of neuronal behavior. These approaches complement traditional modeling techniques, offering new ways to explore the relationships between ion channel dynamics, neuronal excitability, and network function.

The continuing evolution of the Hodgkin-Huxley model underscores its enduring importance as a foundational tool in neuroscience. By addressing its challenges and limitations, researchers continually expand our understanding

of the intricate dynamics of neuronal function and the underlying principles of brain activity.

## Chapter 2: Summary

The Hodgkin-Huxley model is a landmark in neuroscience. It offers a quantitative framework to understand the ionic mechanisms underlying action potentials. This model, developed by Alan Hodgkin and Andrew Huxley in the early 1950s, describes how sodium and potassium ions generate and propagate electrical signals in neurons, revolutionizing our understanding of neural function.

The impact of the Hodgkin-Huxley model extends far beyond its initial application to the squid giant axon. It laid the groundwork for computational neuroscience, enabling the simulation of neuronal behavior and neural networks. The model's principles have also been instrumental in biomedical research, in studying neurological disorders such as epilepsy and chronic pain, and in pharmacology, where it helps predict drug effects on ion channels.

Looking ahead, integrating the Hodgkin-Huxley model with emerging technologies and data from molecular biology promises to refine our understanding of neuronal dynamics further. Advances in high-resolution imaging, optogenetics, and high-throughput electrophysiology will enhance the model's applicability and precision. Additionally, incorporating insights from artificial intelligence and machine learning can uncover new patterns in neural data, leading to more sophisticated and predictive models.

Future innovations will address the model's limitations, such as incorporating more types of ion channels, accounting for synaptic inputs, and adapting the model to human neurons' complexity. These advancements will continue to build on the Hodgkin-Huxley model's legacy, ensuring its relevance in driving forward neuroscience research and applications.



## Chapter 2: Learning activities

### Learning Activity 2.1

Escape rooms are an effective educational tool for several reasons:

- **Engagement and Motivation:** Escape rooms are inherently fun and engaging, capturing students' interest and motivating them to participate actively. The immersive experience makes learning enjoyable, encouraging students to invest effort and energy in solving challenges.
- **Collaboration and Teamwork:** Escape rooms require participants to work together to solve puzzles and achieve a common goal. This promotes teamwork, communication, and collaboration skills, as students must share ideas, listen to each other, and coordinate their actions.
- **Critical Thinking and Problem-Solving:** The puzzles and challenges in escape rooms are designed to be complex and thought-provoking, encouraging students to use critical thinking and problem-solving skills. They must analyze clues, make connections, and think creatively to overcome obstacles.
- **Application of Knowledge:** Escape rooms can be tailored to include subject-specific content, allowing students to apply what they have learned in a practical, hands-on way. This reinforces their understanding and helps them see the relevance of their knowledge in real-world scenarios.
- **Engaging Multiple Learning Styles:** Escape rooms incorporate activities catering to different learning styles, including visual, auditory, and kinesthetic. This ensures that all students can engage with the material in a way that suits their preferred learning method.
- **Time Management and Decision-Making:** The time-limited nature of escape rooms teaches students to manage their time effectively and make quick decisions. They learn to prioritize tasks, allocate resources, and work efficiently under pressure.



- **Assessment and Feedback:** Escape rooms can be an informal assessment tool, allowing educators to observe students' skills and behaviors. The immediate feedback from the success or failure of solving a puzzle provides valuable insights into students' understanding and areas for improvement.
- **Emotional and Social Learning:** Escape rooms' interactive and collaborative nature helps students develop emotional and social skills. They learn to cope with frustration, celebrate successes, support peers, and build resilience through repeated trials and errors.
- **Real-World Skills:** The skills developed in escape rooms, such as critical thinking, teamwork, communication, and problem-solving, are highly valuable in real-world contexts. Students can transfer these skills to various academic and professional situations.
- **Customization and Versatility:** Escape rooms can be customized to fit any educational subject or theme, making them a versatile tool for a wide range of topics and age groups. Educators can design puzzles and challenges that align with specific learning objectives and curriculum standards.

We propose the following escape room based on Qualtrics and the chapter on Huxley-Hodgkin modeling from the book *Physiology for Engineers: Applying Engineering Methods to Physiological Systems (Biosystems & Biorobotics, 13)*, 1st ed. 2016.

Link: [https://und.qualtrics.com/jfe/form/SV\\_dai8rHdSF9Z4Sr4](https://und.qualtrics.com/jfe/form/SV_dai8rHdSF9Z4Sr4)

---

## Learning Activity 2.2

Continuing with the buzz group educational technique, have groups of 3 students create a Pugh chart of the neural modeling tools currently available.

A Pugh chart, also known as a decision matrix or selection matrix, is a tool used to compare multiple options against a set of criteria to



determine the best choice. Named after its creator, Stuart Pugh, this method helps make structured and objective decisions by evaluating alternatives based on specific attributes or performance indicators.

***Structure of a Pugh Chart***

- 1. **Criteria:** The vertical axis lists the criteria against which each option will be evaluated.
- 2. **Options:** The horizontal axis lists the different alternatives or options being compared.
- 3. **Scoring:** Each option is scored against each criterion. Scores can be numerical or symbolic (e.g., +, -, 0), indicating whether an option is better, worse, or the same compared to a baseline.
- 4. **Baseline:** One option is typically chosen as a baseline or reference point against which others are compared.
- 5. **Summarization:** The scores are summed or analyzed to determine the overall ranking of each option.

***Example of a Pugh Chart***

Let's create an example for evaluating neural modeling tools:

Criteria	Tool A	Tool B	Tool C	Baseline (Tool A)
Ease of Use	0	+	-	0
Accuracy	+	0	+	0
Computational Cost	-	+	0	0
Documentation	+	-	+	0
Community Support	0	+		0
Total Score	+1	+2	0	0

In this example, "+" means better than the baseline, "-" means worse, and "0" means equal to the baseline. Tool B scores the highest overall.

Benefits of Pugh Charts for Educational Active Learning:

- **Structured Decision-Making:** Pugh charts provide a clear and structured approach to comparing multiple options, teaching students how to evaluate choices systematically.
- **Critical Thinking:** Students must define relevant criteria, analyze each option against these criteria, and make justified evaluations, promoting critical thinking and analytical skills.
- **Collaboration:** Creating a Pugh chart in a group setting encourages discussion, debate, and consensus-building, enhancing teamwork and communication skills.
- **Real-World Application:** Using Pugh charts simulates decision-making processes used in professional settings, helping students understand how to apply theoretical knowledge to practical scenarios.
- **Visual Learning:** The visual representation of the comparison helps understand and interpret complex information, catering to visual learners.
- **Active Participation:** Engaging students in creating and discussing Pugh charts ensures active participation, making the learning process interactive and dynamic.
- **Objective Evaluation:** The method encourages objective evaluation based on defined criteria rather than subjective preferences, fostering a more impartial and fair decision-making process.
- Overall, Pugh charts are an effective educational tool that can enhance active learning by promoting structured, collaborative, and critical evaluation of various options or concepts.

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## Learning Activity 2.3

A brainstorming activity is a creative and collaborative process to generate a wide range of ideas, solutions, or concepts related to a specific topic or problem. It begins with clearly defining the topic or issue to be addressed, ensuring that all participants understand the session's focus. Participants are then typically divided into small groups, although the activity can also be conducted



with the whole class, depending on its size and nature. The idea generation phase follows, where participants are encouraged to share their ideas freely and spontaneously, prioritizing quantity over quality initially. Techniques like "yes, and..." are used to build on each other's ideas, fostering a supportive environment where all contributions are valued.

A critical rule during brainstorming is to suspend judgment and criticism to maintain an open and encouraging atmosphere. All ideas are documented on a visible medium like a whiteboard, flip chart, or digital platform. After the initial phase, ideas are reviewed and refined, with similar ideas grouped and promising concepts further developed. The group then evaluates and prioritizes the most feasible, innovative, or relevant ideas using impact, feasibility, and relevance criteria. The final step involves developing action plans for implementing the selected ideas, assigning tasks, and setting timelines for execution.

Brainstorm activities encourage creativity by promoting out-of-the-box thinking and exploring new ideas. They foster collaboration, enhance teamwork and communication among participants, and actively involve everyone, increasing their motivation and investment in the process. By drawing on the collective knowledge and experience of the group, brainstorm activities generate diverse perspectives and lead to innovative solutions and effective strategies for addressing challenges. For instance, in a session aimed at improving school lunches, students might be divided into small groups to generate and build on ideas using the "yes, and..." technique, then refine and prioritize the best concepts before developing an implementation plan. This structured yet flexible approach ensures a productive and engaging brainstorming experience.

We propose the following brainstorm activity with the theme of understanding the basics of neuron anatomy and functionality to design a better neuron.



## Chapter 2: Lab introduction

In this series of lab exercises, you will explore the fundamental principles of neuroscience through practical applications using advanced engineering tools. These labs are designed to provide hands-on experience with MATLAB and Simulink, enabling you to deepen your understanding of neuron function and modeling. You will begin by studying the structure and communication mechanisms of neurons, the brain's fundamental building blocks.

In the first lab, you will access and follow instructions to clone and work with a provided example locally on your machine. This practical task will help you become familiar with the tools and datasets needed for neuron analysis and visualization. By engaging with this hands-on example, you will build a foundational understanding of the methodologies used in neuroscience research.

In the second lab, you will delve into the Izhikevich (IZH) Model, a mathematical model introduced by Eugene M. Izhikevich in 2003 to replicate various spiking and bursting behaviors observed in neurons. Using Simulink, you will create and simulate the IZH model, exploring different firing patterns of neurons. This exercise will provide you with practical experience in modeling complex neuronal behaviors and a deeper understanding of neuronal dynamics.



# Chapter 2: Lab Example 1



## *Introduction*

The example below can be accessed either by following the instructions or by following them to clone it to your local machine.

## *Prerequisites*

- Windows Subsystem for Linux (WSL)
- Visual Studio Code (VS Code)
- Git -
- Python 3.10 or higher
- [Neuron](#)

## *Step-by-Step Guide*

### 1. Install WSL and VS Code

- **WSL:** Follow the [official Microsoft guide](#) to install WSL.
- **VS Code:** Download and install [VS Code](#).

### 2. Open VS Code with WSL

1. Open VS Code.
2. Press Ctrl+Shift+P to open the command palette.
3. Type WSL: New Window and select it to open a new VS Code window with a WSL session.

### 3. Clone the GitHub Repository

1. Open the terminal in VS Code (using WSL).
2. Navigate to your desired directory:
3. `cd /path/to/your/directory`
4. Clone the GitHub Repository
5. `git clone https://github.com/your-username/your-repo.git`
6. Navigate to the Chapter repo you want to run examples for
7. `cd chapter repo`
8. Run the examples
9. `python3 example.py`

For this example, you will be using the [neuronHH.py](#) model.

## *Hodgkin-Huxley Model Example:*

### *Import Libraries:*

- **neuron.h, gui**: Imports NEURON simulation environment and GUI components.
- **numpy**: Used for numerical calculations, especially arrays and mathematical functions.
- **matplotlib.pyplot**: Used for plotting graphs and visualizations.

```
from neuron import h, gui
import numpy as np
from matplotlib import pyplot as plt
```

### *Create Sections:*

- **soma** and **dend**: Creates two sections, representing the soma and dendrite of a neuron.
- **dend.connect(soma(1))**: Connects the dendrite to the soma at the end (position 1) of the soma.

```
# Create sections
soma = h.Section(name='soma')
dend = h.Section(name='dend')

# Topology
dend.connect(soma(1))
```

### *Define Geometry:*

- Sets the length (L) and diameter (diam) of the soma and dendrite sections in microns

```
# Geometry
soma.L = soma.diam = 12.6157 # microns
dend.L = 200 # microns
dend.diam = 1 # microns
```

## *Define Biophysics:*

- Sets the biophysical properties for all sections: axial resistance (Ra) and membrane capacitance (cm).
- **soma.insert('hh')**: Inserts the Hodgkin-Huxley model into the soma.
- Sets sodium, potassium, leak conductances, and the leak reversal potential for the soma.
- **dend.insert('pas')**: Inserts a passive current mechanism into the dendrite.
- Sets passive conductance and leak reversal potential for the dendrite.

```
# Biophysics
for sec in h.allsec():
    sec.Ra = 100      # Axial resistance in Ohm * cm
    sec.cm = 1        # Membrane capacitance in micro
Farads / cm^2

soma.insert('hh')    # Insert active Hodgkin-Huxley
current in the soma
for seg in soma:
    seg.hh.gnabar = 0.12 # Sodium conductance in
S/cm2
    seg.hh.gkbar = 0.036 # Potassium conduct-ance
in S/cm2
    seg.hh.gl = 0.0003   # Leak conductance in
S/cm2
    seg.hh.el = -54.3    # Reversal potential in
mV

dend.insert('pas')    # Insert passive current in the
dendrite
for seg in dend:
    seg.pas.g = 0.001   # Passive conductance in
S/cm2
    seg.pas.e = -65     # Leak reversal poten-tial
mV
```

## ***Simulation:***

**h.IClamp(dend(1)):** Places a current clamp at the end of the dendrite.

- **delay:** Delay before the stimulus starts (5 ms).
- **dur:** Duration of the stimulus (1 ms).
- **amp:** Amplitude of the stimulus (0.1 nA).

```
# Stimulation
stim = h.IClamp(dend(1))
stim.delay = 5
stim.dur = 1
stim.amp = 0.1
```

## ***Recording Vectors:***

- Creates vectors to record membrane potential (v\_vec) and time (t\_vec).
- Records the membrane potential at the middle of the soma (soma(0.5)) and the time from the simulation.

```
# Recording vectors
v_vec = h.Vector() # Membrane potential vector
t_vec = h.Vector() # Time stamp vector
v_vec.record(soma(0.5)._ref_v)
t_vec.record(h._ref_t)
```

## ***Run Simulation:***

- Sets the simulation duration (simdur) to 25 ms
- Runs the simulation

```
# Run simulation
simdur = 25.0
h.tstop = simdur
h.run()
```

## ***Plot Results:***

- Plots the membrane potential of the soma over time

- Annotates the plot for explanation

```
# Plot membrane potential with explanation
plt.figure(figsize=(8, 4))
plt.plot(t_vec, v_vec)
plt.xlabel('time (ms)')
plt.ylabel('mV')
plt.annotate('Membrane potential of soma over
time', xy=(0.5, 0.95), xycoords='axes fraction',
ha='center')
plt.show()
```

User Input to Proceed Through Graphs (User prompts found in Fig 2.16):

- Prompts the user to decide whether to vary the amplitude of the current.
- If the user inputs "yes," varies the amplitude of the stimulus in steps and plots the effect on the membrane potential of the soma.
- Prompts the user to decide whether to visualize dendrite activity.
- If the user inputs "yes," it records and plots the membrane potential of both the soma and the dendrite for varying stimulus amplitudes.
- Prompts the user to decide whether to test the effects of nseg (number of segments) on the dendritic signal.
- If the user inputs "yes," tests and plots the effects of different nseg values on the membrane potential of the soma and dendrite, calculating and displaying the average error between high and low-resolution simulations.
- The script exits if the user decides not to proceed at any prompt.

You must follow some prompt results as you see each graph to either process “yes” or not to proceed with “no” with the results.

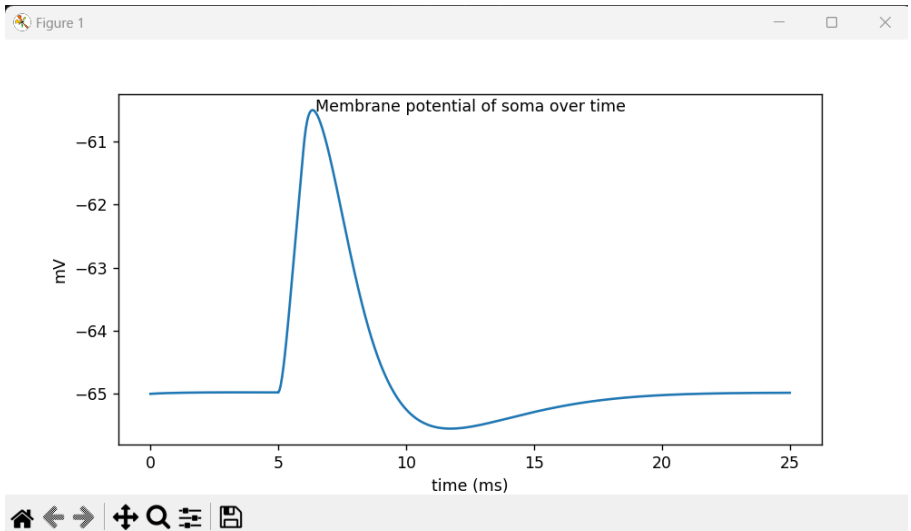


Figure 2.12: Membrane Potential of some over time

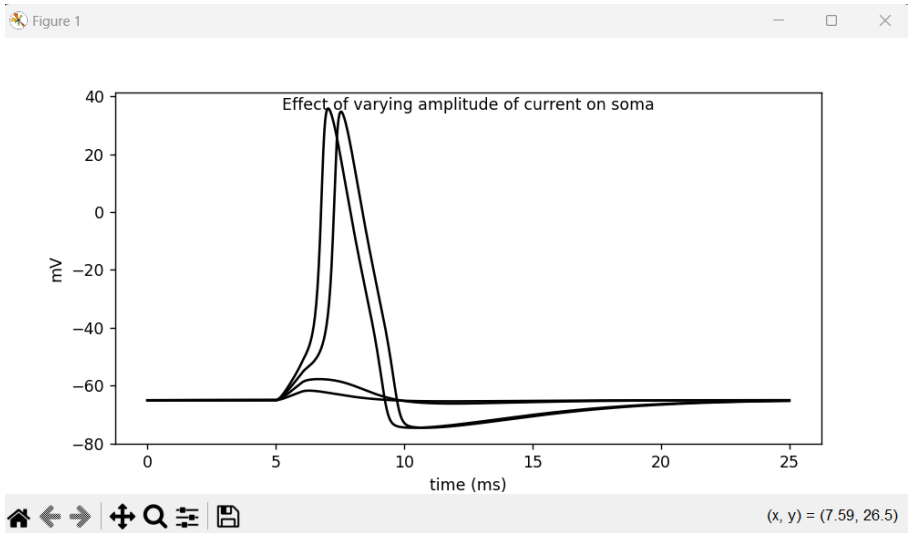


Figure 2.13: Effect of varying amplitude of current on soma

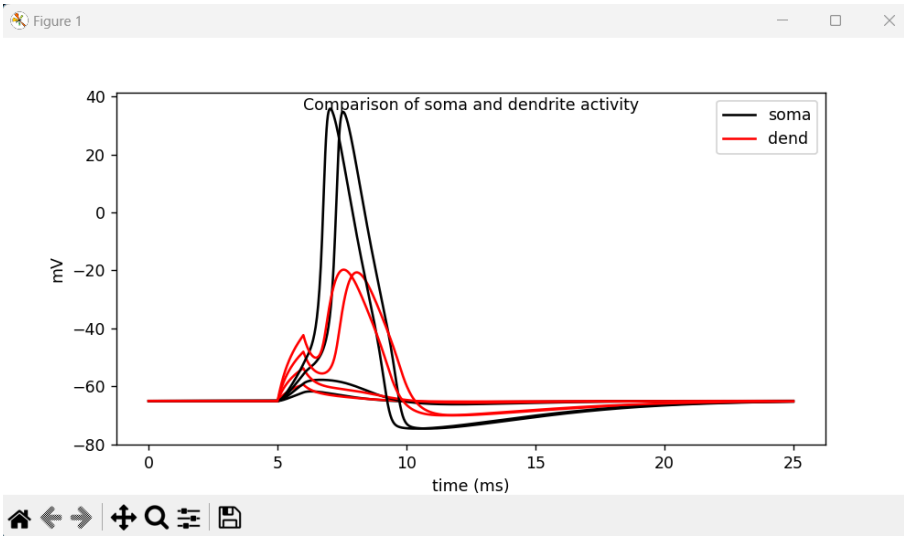


Figure 2.14: Comparison of soma and dendrite activity

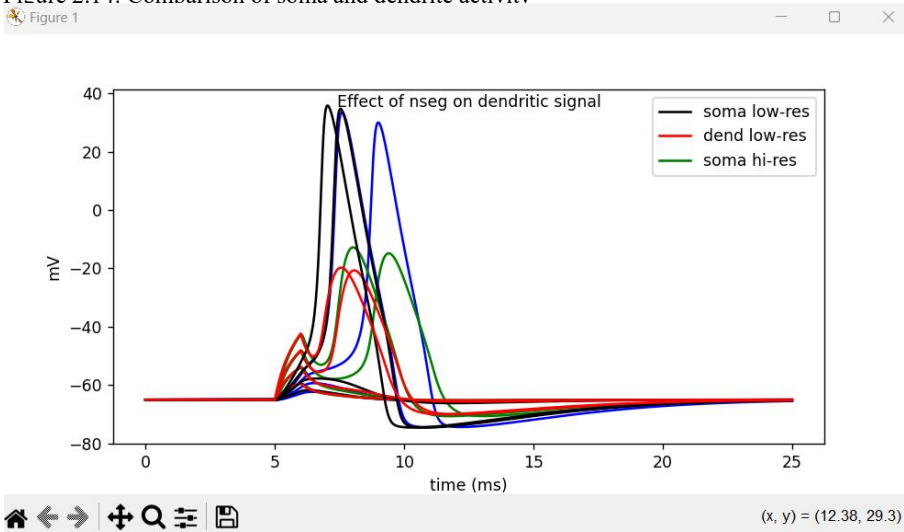


Figure 2.15: Effect of nseg on dendritic signal

Once you see the final graph (Fig 2.15), you will also see the Average percent error as an output in the terminal:

```
ts/Chapter_2_Labs/lab3_Neuron/neuronHH.py
Proceed to vary amplitude of current? (yes/no)
yes
Proceed to visualize dendrite activity? (yes/no)
yes
Proceed to test the effects of nseg on dendritic signal? (yes/no)
yes
Average error = 2.6101668670905465
```

Figure 2.16: Terminal User Prompts

To do more advanced modifications, you can always go into the code and modify dendrite and soma equations for more advanced representations of them!

You have learned how to create and manipulate a basic neuronal model using the NEURON simulation environment in this lab. Specifically, you constructed a simple model consisting of soma and dendrite, defined the biophysical properties of these sections, and inserted active and passive conductances to simulate realistic neuronal behavior.

You applied current stimulation to observe how the soma's membrane potential responds over time, then explored the effects of varying the current amplitude on the soma's activity. Additionally, you visualized and compared the membrane potential changes in both the soma and dendrite, demonstrating the spatial differences in signal propagation within the neuron.

Finally, you experimented with adjusting the number of segments (nseg) in the dendrite to understand its impact on the accuracy of signal representation. This exercise highlighted the importance of model resolution in achieving accurate simulations of neuronal activity.

This lab provided hands-on experience with neural modeling and an understanding of how biophysical properties and model parameters influence neuronal behavior in computational simulation.



# Chapter 2: Lab Example 2

## Overview



This Lab Example will look at the Izhikevich (IZH) Model. The Izhikevich model is a mathematical model of a neuron, like that of Hodgkin-Huxley's, and it is designed to replicate a wide variety of spiking and bursting behaviors observed in neurons. Eugene M. Izhikevich introduced it in 2003 [34] as a more detailed model and alternative to the Hodgkin-Huxley model. In this lab, we will use Simulink to create the IZH model and then look at different firing patterns of a neuron [35]. The following system of ordinary differential equations describes the IZH Model.

The membrane potential equation

$$\frac{dv}{dt} = 0.04v^2 + 5v + 140 - u + I \quad (2.5)$$

The recovery variable

$$\frac{du}{dt} = a(bv - u) \quad (2.6)$$

The model also includes an after-spiking resetting condition.

$$\text{if } v = 30 \text{ mV, then } \begin{cases} v \leftarrow c \\ u \leftarrow u + d \end{cases} \quad (2.7)$$

Here is a breakdown of each variable in the equation and how they work.

## Variables

$v$

- Represents the membrane potential of the neuron.

- Measured in millivolts (mV).
- The variable indicates the neuron's voltage at any given time.
- When  $v$  reaches a threshold (e.g., 30 mV), the neuron has fired an action potential (spike).

*u*

- Represents the membrane recovery variable.
- It accounts for  $K^+$  (potassium) activation and inactivation of  $Na^+$  (sodium) ionic currents.
- It helps in modeling the refractory period of the neuron, during which the neuron is less likely to fire another spike.
- Influences the rate at which the membrane potential returns to its resting state after a spike.

*I*

- Represents the input current to the neuron.
- It can be thought of as the external stimulus or synaptic input the neuron receives.
- It influences the neuron's membrane potential and can cause it to reach the threshold to fire a spike.

*a*

- The time scale of the recovery variable  $u$ .
- Controls how quickly  $u$  responds to changes in  $v$ .

*b*

- Sensitivity of the recovery variable  $u$  to the membrane potential  $v$  subthreshold fluctuations.
- Determines how strongly  $u$  is coupled to  $v$ .

*c*

- The after-spike reset value of the membrane potential  $v$ .
- When the membrane potential  $v$  reaches the threshold (e.g., 30 mV), it is reset to  $c$ .

*d*

- After-spike reset increment of the recovery variable  $u$ .

- When the membrane potential  $v$  is reset,  $u$  is incremented by  $d$ .
- This helps to model the effect of spike-triggered adaptation, where the neuron's excitability is reduced after firing.

## ***How it works***

### ***Membrane Potential Dynamics***

- The first equation models the membrane potential dynamics  $v$ . It includes a quadratic term  $0.04v^2$ , a linear term  $5v$ , and constant terms that drive the membrane potential.
- The term  $-u$  represents the inhibitory effect of the recovery variable on the membrane potential.
- The input current  $I$  can depolarize (excite) or hyperpolarize (inhibit) the membrane potential.

### ***Recovery Variable Dynamics***

- The second equation describes the dynamics of the recovery variable  $u$ . It adjusts  $u$  based on the current value of  $v$  and the difference between  $bv$  and  $u$ .
- The parameter  $a$  controls the time scale, while  $b$  determines the sensitivity  $u$  to  $v$ .

### ***After-Spike Resetting***

- When the membrane potential  $v$  reaches a threshold (30 mV), it is reset to a lower value  $c$ , simulating the neuron firing an action potential.
- Simultaneously, the recovery variable  $u$  is incremented by  $d$ , increasing its value to reflect the refractory period where the neuron is less likely to fire again immediately.

By adjusting the parameters  $a$ ,  $b$ ,  $c$ , and  $d$ , the IZH model can replicate various types of neuronal behavior, making it versatile and efficient for simulating neuronal networks. Here is a figure taken from Izhikevich et al. (2003) that shows some of the different types of spiking patterns that the model can replicate. In this lab, we will replicate a YouTube tutorial from MATLAB Ambassador. YouTube is an excellent resource for tutorials on using different engineering tools.

## Requirements

- Simulink
- MATLAB
- YouTube

## Steps

First, open MATLAB. Then, use this link to find the YouTube page for the video Simulating a Neuron by the MATLAB Ambassador.

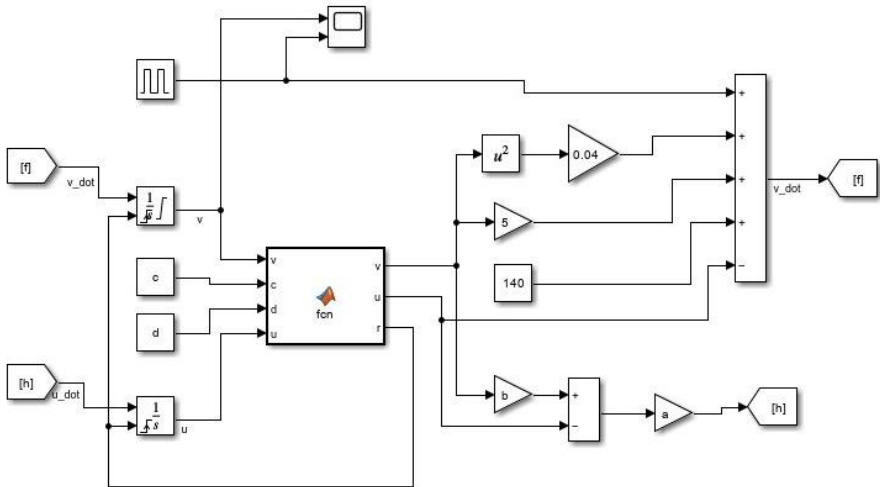
[https://youtu.be/NnZlGC1\\_I0M?si=EvFK8it5b39wfShn](https://youtu.be/NnZlGC1_I0M?si=EvFK8it5b39wfShn)

In the video, the caption includes a link to a Google Drive folder with the files needed to complete this lab. Here is the link as well.

<https://drive.google.com/drive/folder...>

### Izhikevic Model

$$\begin{cases} \dot{v} = 0.04v^2 + 5v + 140 - u + I = f(u, v, I) \\ \dot{u} = a(bv - u) = h(u, v) \end{cases}$$



Once you have the folder open, download the NeuronParameters.m file. This MATLAB script will give us our parameters for the variables discussed in the IZH model. Once you download the file, save it and open it in your MATLAB as a new script. You can also double-click the file to open it in MATLAB. Once you open the MATLAB script, click run to ensure no errors.

After this, go back to Google Drive and download the NeuronVideo2.slxc file. This is going to be the Simulink model. You can open it two ways. The first way is to double-click on the file and automatically open it in Simulink. The second way is to save the file, navigate to Simulink under the Home tab in MATLAB, click open under the simulation file, and then click the file. Once you have opened the Simulink file, it should look like Fig. 2.16.

### ***Simulink Model Components Description***

Here is a breakdown of the critical components of the Simulink model:

#### ***Input Block (I):***

- Represents the input current to the neuron.

#### ***Membrane Potential Equation Implementation:***

- Blocks calculate  $0.04v^2$ ,  $5v$ , and the constants  $140$  and  $-u$ .
- The sum of these components and the input current  $I$  gives  $dv/dt$

#### ***Recovery Variable Equation Implementation:***

- Blocks calculate  $a(bv-u)$  to determine  $du/dt$

Figure 2.16: Simulink IZH model

#### ***Function Block (Fcn):***

- Handles the after-spike resetting condition. When  $v$  reaches  $30$  mV, it resets  $v$  to  $c$  and increments  $u$  by  $d$ .

#### ***Integrator Blocks:***

- Integrate  $dv/dt$  and  $du/dt$  to update  $v$  and  $u$  over time.

#### ***Output Blocks:***

- Display the membrane potential  $v$  and the recovery variable  $u$ .

Now that you have all the files and understand how they work, watch the YouTube video where you will model tonic spiking and bursting. Click the scope box to view the neurons' spiking pattern.

Next, we will take this lab further and model more spiking patterns. We are going to model the inhibition-induced spiking and spiking latency. You will first need to return to your Neuron Parameters code in MATLAB and add the following parameters for the variables.

<b>a</b>	-0.02
<b>b</b>	-1
<b>c</b>	-60
<b>d</b>	8
<b>I</b>	80

Then, you will need to change T to equal 3. This means that MATLAB will pull the parameters from row three of the parameter's matrix. Click Run. Then go to Simulink and click Run on your model. You must click Run in MATLAB before rerunning the Simulink model. Double-click the Scope box to see the firing pattern.

Inhibition-induced spiking, also known as post-inhibitory rebound speaking, is a phenomenon where a neuron generates action potentials in response to inhibitory input. This behavior is counterintuitive because inhibition typically

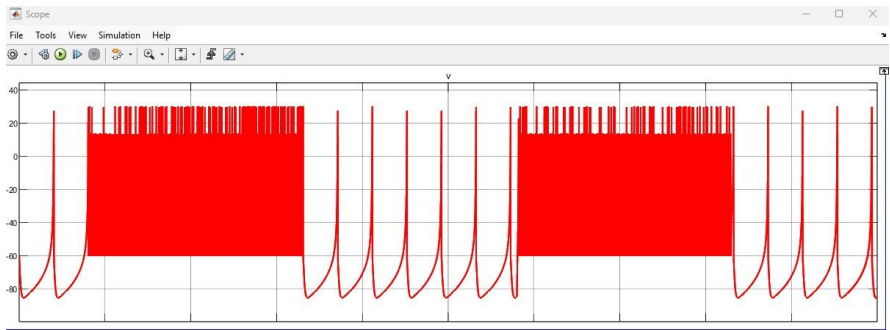


Figure 2.17: Inhibition-induced spiking scope box result

reduces neuronal activity, yet it can trigger spiking in this case. The mechanism for inhibition-induced spiking involves:

1. Inhibitory input that hyperpolarizes the neuron's membrane potential
2. Deactivation of inward current where low threshold calcium channels or hyperpolarization-activated cation channels become deactivated
3. Rebound Depolarization: When the inhibitory input is removed, the neuron experiences rebound depolarization. This occurs because the previously de-inactivated ion channel is activated, allowing an influx of positive ions.
4. Action Potential Generation, where the rebound depolarization is strong enough, can bring the membrane potential above the threshold and create an action potential.

Inhibition-induced spiking generates rhythmic activity patterns in circuits responsible for locomotion and respiration. Additionally, this type of firing can help synchronize the activity of neural networks (Chapter 3), contributing to the coordination of the timing of neural processing. This type of firing pattern shows that an inhibitory signal is just as crucial as excitatory signaling.

Now, let’s enter the following parameters for a spiking latency.

<b>a</b>	0.02
<b>b</b>	0.2
<b>c</b>	-65
<b>d</b>	6
<b>I</b>	7

Remember, you must change the T variable in MATLAB to the appropriate row in the matrix you want to pull from and click run on the MATLAB script before running the Simulink model.

Spike latency in neuroscience refers to the time delay between the onset of a stimulus and the generation of an action potential (spike) by a neuron. This measure is crucial for understanding how neurons respond to external stimuli and process information. Spike latency plays an essential role in temporal encoding, as it helps neurons communicate the timing of sensory information.

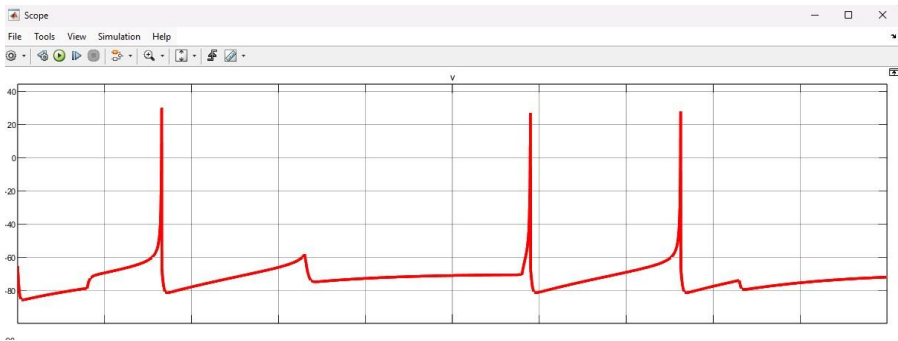


Figure 2.18: Resonator scope box result

For example, in sensory systems, the latency of a spike can reflect how quickly a stimulus is processed, with shorter latencies indicating faster responses. This measure provides valuable insight into the efficiency and speed of neural circuits, which is particularly important for tasks requiring quick reflexes or rapid processing.

Additionally, spike latency affects neural coding by influencing how information is represented and integrated within the brain. Variations in latency can be used to assess changes in neural function due to various factors, such as diseases or experimental manipulations. Moreover, alterations in spike latency can signal neural plasticity and learning, indicating modifications in synaptic connections or neural pathways. Spike latency is a critical parameter for understanding the dynamics of neuronal responses and their contributions to sensory perception, motor control, and cognitive functions.

That is the end of this lab example. You are encouraged to research different firing patterns that can be replicated using this model and try to use them in MATLAB and Simulink.

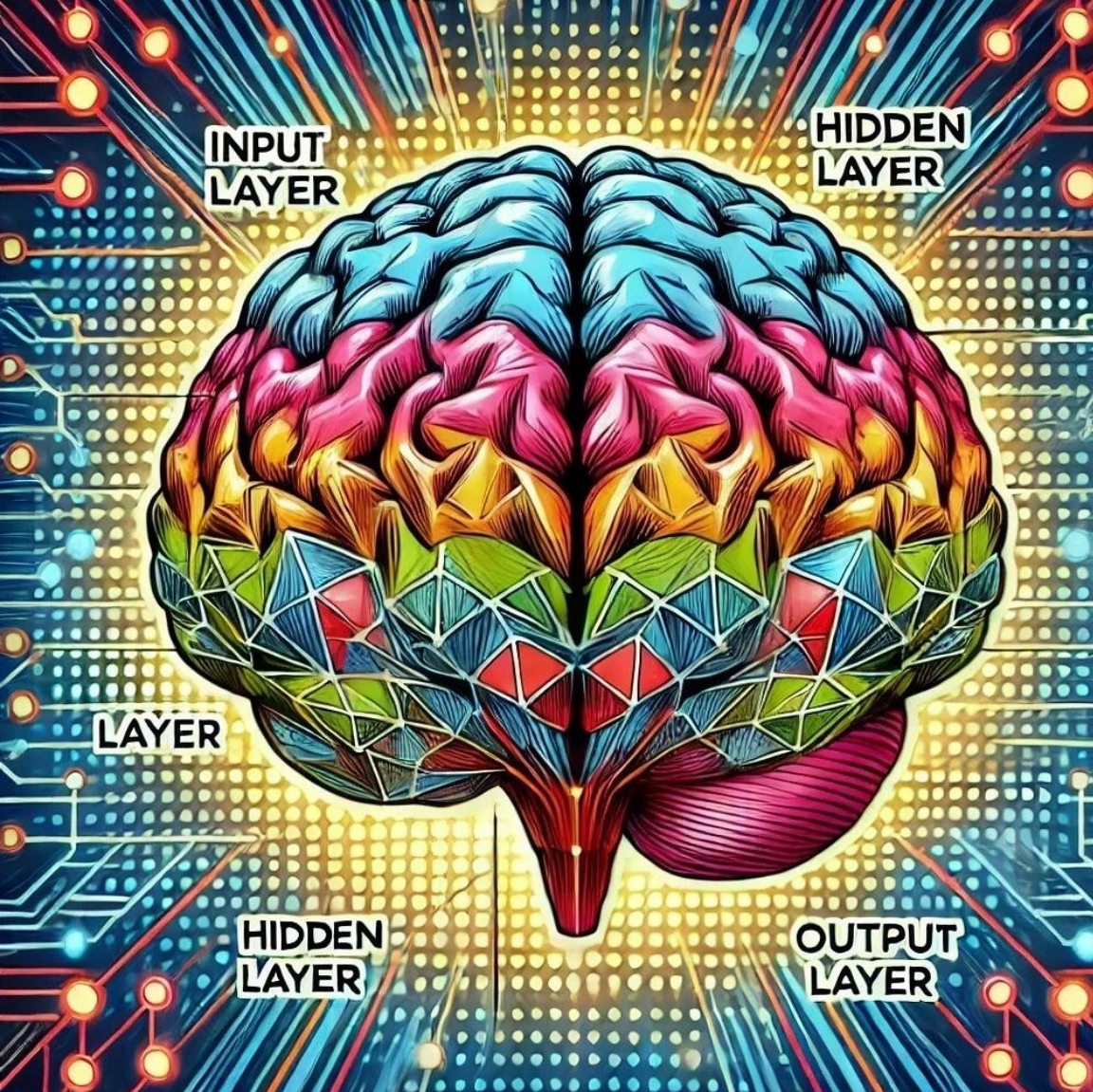
## Acknowledgments

We want to express our sincere gratitude to the MATLAB Ambassador for creating the instructional YouTube video "Simulating a Neuron." This video has been invaluable in guiding us through implementing and understanding the Izhikevich neuron model using Simulink. The clear explanations and detailed

walkthrough provided in the video have greatly enhanced our ability to model various neuronal firing patterns and apply these concepts in our lab exercises. We also extend our thanks to the community of educators and content creators who continue to share their knowledge and expertise through platforms like YouTube, making advanced learning accessible and engaging for students and professionals worldwide.

Thank you for your contribution to computational neuroscience and educational outreach.





## Chapter 3

# Neural Networks: The Brain's Digital Doppelgangers

# Introduction and Learning Objectives

Neural networks are transforming our world in ways that were once thought impossible. They enable machines to perform tasks that previously required human intelligence, such as recognizing faces, translating languages, or even driving cars [36]. This raises several critical questions: How do neural networks function? What makes them so powerful? Can they genuinely mimic human intelligence? Understanding these concepts is essential for neuroengineering students, as neural networks are foundational to artificial intelligence (AI) and neurotechnology advancements.

This chapter will delve into the basics of neural networks, exploring their structures, learning processes, and applications. We will cover the history of neural networks, their evolution, and their profound impact on fields like healthcare. By the end of this chapter, you will be able to:

- 1. Understand the fundamental architecture and components of neural networks.*
- 2. Explain the process of training neural networks, including critical algorithms and techniques.*
- 3. Identify and describe different types of neural networks and their specific applications.*
- 4. Discuss the ethical considerations and potential biases in developing and deploying neural networks.*
- 5. Analyze real-world examples of neural network applications, particularly in healthcare.*

Neural networks are composed of interconnected layers of artificial neurons. These networks learn by adjusting the connections (weights) between neurons based on the data they process. This process resembles how the human brain adjusts synaptic strengths to learn from experiences [37]. The ability of neural networks to learn and adapt makes them incredibly versatile and powerful tools.

# Historical Evolution of Neural Networks

Understanding the historical evolution of neural networks provides valuable context for their current capabilities and future potential. The journey of neural networks is marked by periods of innovation, skepticism, and resurgence.

The concept of artificial neurons dates back to the 1940s. Warren McCulloch and Walter Pitts proposed a mathematical model of a neuron, which could perform simple logical operations. Their work laid the foundation for artificial neural networks [38]. In 1958, Frank Rosenblatt introduced the perceptron, an early type of neural network that could learn to classify data into two categories. Despite its simplicity, the perceptron shown in Fig. 3.1 [39] demonstrated the potential of machine learning [40].

The initial excitement around neural networks was followed by periods of skepticism, known as AI winters. In 1969, Marvin Minsky and Seymour Papert published a book titled "Perceptrons," highlighting the limitations of single-layer perceptrons. This criticism led to declining funding and interest in neural network research [41]. However, the limitations of other AI approaches eventually became apparent, leading researchers back to neural networks.

The resurgence of neural networks began in the 1980s with the development of backpropagation. Backpropagation allowed networks to learn complex, non-linear relationships in data. Key figures such as Geoffrey Hinton, Yann LeCun, and Yoshua Bengio were pivotal in advancing neural network research [36], [42].

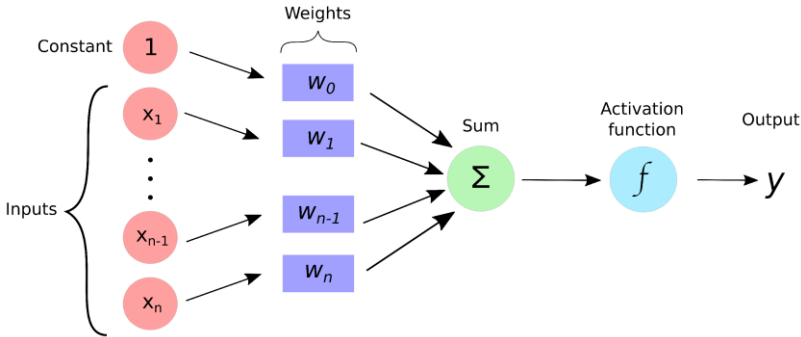


Figure 3.1: Perceptron Model showing the structure of the perceptron with inputs, weights, sum, activation function, output [39].

### Machine Learning & Deep Learning Algorithms Development Timeline

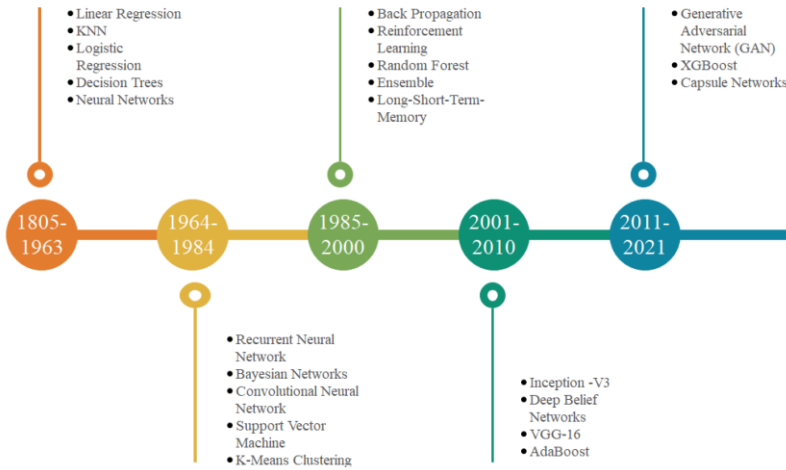


Figure 3.2: Evolution of Neural Networks [45]

Fast forward, 2010s saw numerous breakthroughs in neural network applications. Deep learning models achieved state-of-the-art performance in tasks such as image recognition, natural language processing, and game playing. Notable achievements include:

- **ImageNet Competition:** In 2012, a deep convolutional neural network developed by Hinton's team, AlexNet, won the ImageNet Large Scale Visual Recognition Challenge with a significant margin, showcasing the power of deep learning [43].
- **AlphaGo:** In 2016, Google DeepMind's AlphaGo defeated the world champion Go player, demonstrating the ability of neural networks to master complex strategic games [44].
- **Speech and Language Processing:** Neural networks have revolutionized speech recognition and natural language processing, enabling technologies like virtual assistants (e.g., Siri, Alexa) and machine translation (e.g., Google Translate) [36].

We then transition to the age of GPTs, or Generative Pre-Trained Transformers, a form of Large Language Models (LLMs) that can generate and understand text in our natural language. This breakthrough in neural networks is believed to be the foundation of Artificial General Intelligence (AGI). ChatGPT by OpenAI has reshaped how we work and think to include creativity, such as the chapter images at the beginning of each chapter. This historical context shown in Fig. 3.2 [45] provides a foundation for

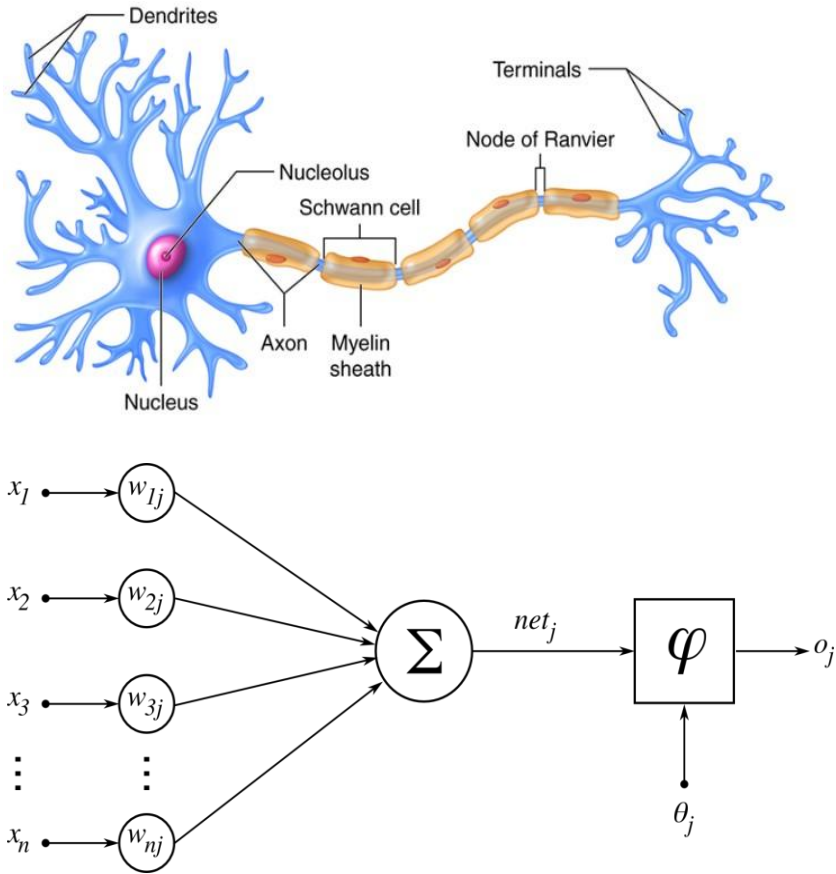


Figure 3.3: Natural Neuron vs. Artificial Neuron [46], [47]

understanding the fundamental architecture and components of neural networks, which we will explore in the next section.

## Fundamentals of Neural Networks

Neural networks, inspired by the structure and function of the human brain, are composed of interconnected layers of artificial neurons shown in Fig. 3.3[46], [47]. These networks can learn from data, recognize patterns, and make decisions, making them incredibly powerful tools in artificial intelligence [48]. The structure we will discuss will focus on neurons, layers, activation functions, and training.

### *Neurons and Layers*

At the heart of a neural network are its neurons or nodes. Each neuron receives inputs, processes them, and produces an output. The processing involves computing a weighted sum of the inputs and applying an activation function to this sum. The neurons are organized into layers, as seen in Fig. 3.4 [49], and can be broadly categorized into input, hidden, and output layers [48].

- **Input Layer:** The entry point of the neural network where the raw data is fed into the system. Each neuron in this layer represents an input feature. For example, in image recognition, each neuron in the input layer might represent a pixel of the image.
- **Hidden Layers:** One or more layers that perform most of the computation. These layers allow the network to learn complex representations of the data. Each neuron in a hidden layer takes inputs from all the neurons in the previous layer, applies a weight to each input, sums them up, and passes the result through an activation function.
- **Output Layer:** The final layer that produces the final prediction or classification. The number of neurons in the output layer corresponds to the number of possible output classes or dimensions. For instance, in a binary classification problem, there would typically be one neuron in the output layer that outputs the probability of the input belonging to the positive class.

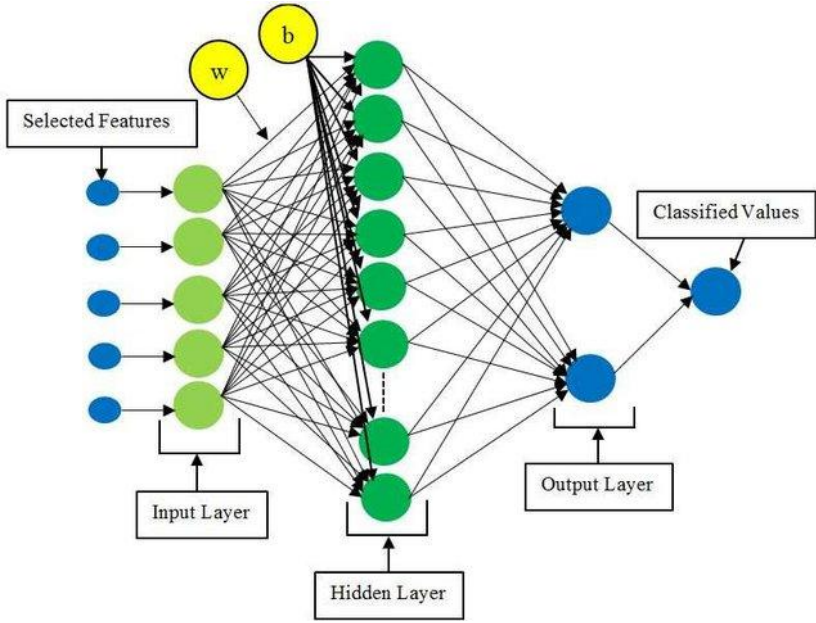


Figure 3.4: Basic Neural Network Architecture [49]

## Activation Functions

Activation functions, as shown in Fig. 3.5 [50], introduce non-linearity into the network, enabling it to learn complex patterns that linear models cannot capture. Without non-linearity, the network would behave like a linear model regardless of its number of layers. Here are some standard activation functions:

- Sigmoid: The sigmoid function maps any real-valued number into the range (0, 1), making it useful for models where the output can be interpreted as a probability. The function is defined as:

**Equation 1**

$$\sigma(x) = \frac{1}{1 + e^{-x}} \quad (3.1)$$

Hyperbolic: hyperbolic tangent function maps any real-valued number into the range (-1, 1). It is similar to the sigmoid function but has the advantage of centering the output around zero. The function is defined as:

**Equation 2**

$$\tanh(x) = \frac{e^x - e^{-x}}{e^x + e^{-x}} \quad (3.2)$$

ReLU (Rectified Linear Unit): The ReLU function is defined as:

**Equation 3**

$$f(x) = \max(0, x) \quad (3.3)$$

It is computationally efficient and helps mitigate the vanishing gradient problem, making it the most commonly used activation function in deep learning [51]. The vanishing gradient problem occurs when the gradients (the guide on adjustments of weights due to loss) used to update neural network weights become very small, effectively preventing the network from learning.

## ***Training Neural Networks***

Training a neural network involves finding the weights that minimize the prediction error on a given task. This process is typically done using supervised learning, where the network learns from labeled examples. The critical steps in training a neural network are:

1. **Forward Pass:** Passing the input data through the network layer by layer, applying weights and activation functions until the output is produced.
2. **Loss Calculation:** Computing the error (loss) between the predicted output and the target using a loss function.
3. **Backpropagation:** Calculating the gradients of the loss with respect to each weight using the chain rule of calculus. This step is crucial as the error is propagated backward through the network, as shown in Fig. 3.6 [52].

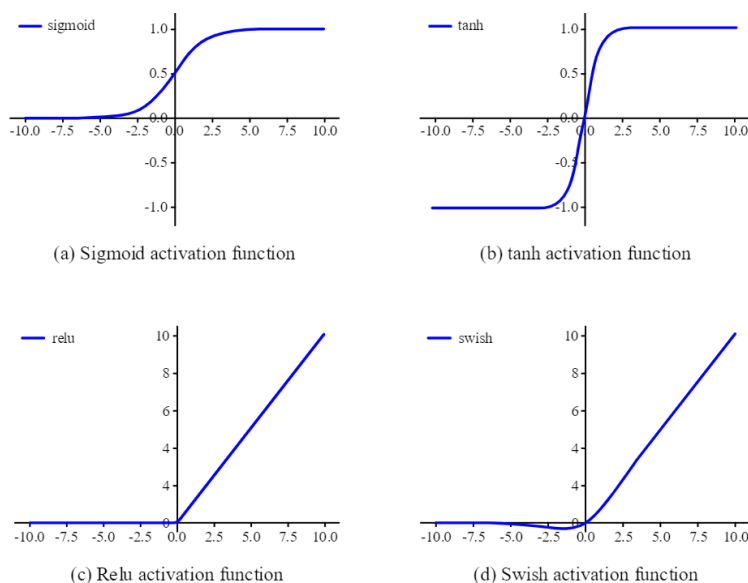


Figure 3.5: Common activation Functions [50]

4. **Gradient Descent:** Updating the weights using an optimization algorithm, typically moving the weights in the direction that reduces the loss. The learning rate controls the size of the weight updates.

By iterating through these steps for many epochs (complete passes through the training data), the network learns to make accurate predictions. Advanced techniques such as batch normalization, dropout, and learning rate scheduling remain vital. At the same time, newer methods like Mixture-of-Experts (MoE), tensor parallelism, and preconditioned gradient descent are increasingly used to enhance training efficiency and performance and prevent overfitting [48]. Having established the fundamental architecture and training processes of neural networks, we can now explore the diverse types of neural networks and their specific applications in various fields.

## Types of Neural Networks

Neural networks, inspired by the human brain, have become foundational tools in artificial intelligence, capable of adapting to various problems through

specialized architectures. Different tasks, such as image recognition or time series analysis, require unique configurations of neural networks to achieve optimal performance [36].

Feedforward Neural Networks (FNNs) are the simplest form of neural networks, where information flows unidirectionally—from input nodes through hidden nodes to output nodes [40]. This straightforward progression makes FNNs particularly effective for problems requiring linear data processing, such as classification tasks or essential image recognition. Their structure typically includes an input layer, one or more hidden layers, and an output layer, which makes them easy to understand and implement [48].

Convolutional Neural Networks (CNNs) are tailored for grid-like data structures like images. CNNs excel in various computer vision tasks, including image and video recognition, image classification, and object detection [43]. The core components of CNNs include convolutional layers, which apply filters to transform input data into feature maps by detecting spatial hierarchies like edges and textures. Activation functions like the Rectified Linear Unit (ReLU) introduce non-linearity, enabling the network to learn complex

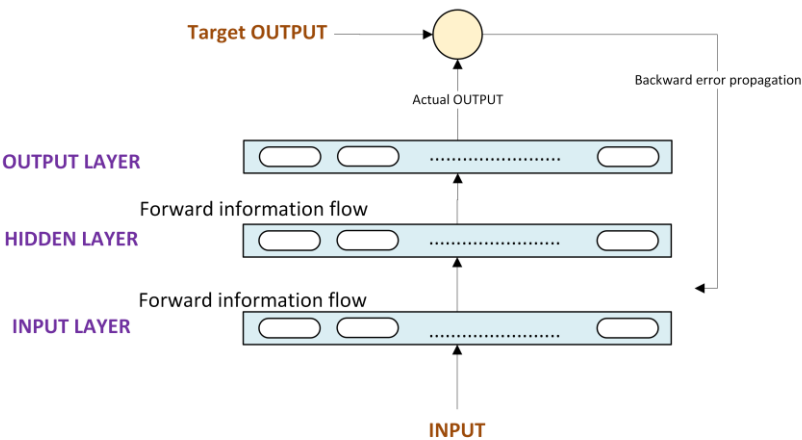


Figure 3.6: Backpropagation Schematic showing the error-backpropagation used to update the model weights based on the gradient [53]

patterns. Pooling layers reduce the dimensionality of feature maps, decrease

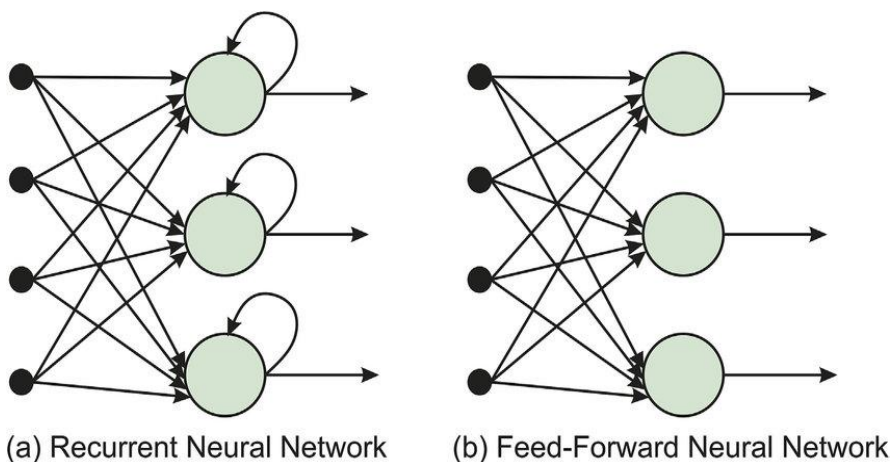


Figure 3.7: RNN and FFNN comparison [54]

computational demands, and prevent overfitting. Fully connected layers, typically at the end of CNN architectures, perform high-level reasoning and make final classifications based on features identified by the convolutional layers [36].

Recurrent Neural Networks (RNNs) are a type of neural network designed to handle sequential data by allowing information to flow through cycles within the network. This means RNNs can remember previous inputs and use this memory to influence future outputs, which is especially useful for tasks like predicting time series data or processing natural language [37]. A schematic comparison of FNN and RNN is shown in Fig. 3.7 [53]. Unlike traditional neural networks that treat each input independently, RNNs have a hidden layer that retains the state of previous inputs, providing the network with historical context essential for making accurate predictions in tasks where the order and timing of data points matter [48].

Long Short-Term Memory (LSTM) networks found in Fig. 3.8 [54] are a specialized type of RNN designed to learn long-term dependencies. LSTMs incorporate memory cells that retain information over extended periods, making them particularly effective in language modeling and other sequence

(c) LSTM

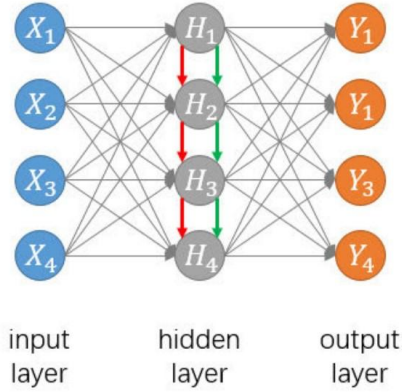


Figure 3.8: Long-Short Term Memory Model [54]

learning tasks [37]. The LSTM architecture includes gates regulating information flow: the forget gate determines what information to discard, the input gate decides what new information to store, and the output gate generates the hidden state for the next step [55].

Transformer networks have revolutionized natural language processing with self-attention mechanisms, which dynamically assign importance to different input parts. This capability enhances performance in language translation, text summarization, and question answering [56]. Transformers use positional encoding to maintain the order of words in a sequence and self-attention mechanisms to evaluate relationships within the data. Transformers consist of encoders, which process the input sequence into continuous representations, and decoders, which generate output sequences step by step [57].

Generative Adversarial Networks (GANs) (Fig. 3.9 [58]) consist of two neural networks, a generator and a discriminator, trained simultaneously. The generator creates data that mimics the training data, while the discriminator differentiates between real and generated data [48]. This adversarial process is

## A. Generative Adversarial Network

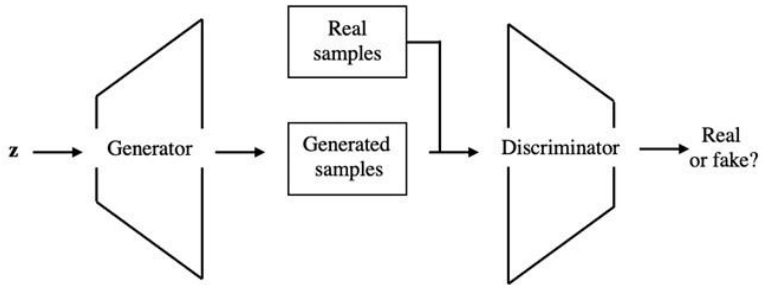


Figure 3.9: Generative Adversarial Network (GAN) Flow Diagram [58]

commonly used to create realistic images, videos, and other data types. As training progresses, the generator improves, producing increasingly realistic data, while the discriminator refines its ability to distinguish real from fake data [59].

With a clear understanding of the various types of neural networks, we can now delve into the feedback mechanisms that enhance their learning and performance. Feedback mechanisms, such as those found in RNNs and attention mechanisms, play a critical role in allowing neural networks to handle sequential data, focus on essential features, and improve overall learning efficiency. These mechanisms are pivotal in applications ranging from natural language processing to time series analysis, illustrating how neural networks continuously evolve and adapt to new challenges. Understanding these feedback processes will further enrich our understanding of neural networks' capabilities and potential for real-world applications.

(b) RNN

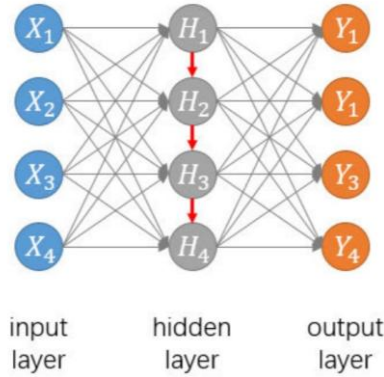


Figure 3.10: Recurrent Neural Network (RNN) diagram [60]

## Feedback Mechanisms in Neural Networks

Feedback mechanisms are essential in specific neural network architectures, particularly in the context of RNNs and other architectures where the output or hidden state of the network is fed back into itself (Fig. 3.10 [60]).

RNNs are designed to handle sequential data by maintaining a hidden state updated at each time step. This hidden state captures information from previous time steps, allowing the network to learn dependencies in the sequence. Training RNNs involves backpropagation through time (BPTT), where gradients are calculated for each time step and accumulated to update the weights. This process can be computationally intensive and prone to issues like the vanishing gradient problem [61].

Beyond RNNs, feedback mechanisms in Neural network architectures incorporate various techniques to enhance learning and performance. Attention mechanisms, for example, allow the network to focus on specific parts of the input sequence, improving tasks like machine translation and text generation by selectively prioritizing relevant information [62]. Residual connections in

deep neural networks create shortcut paths for gradients, which help mitigate the vanishing gradient problem and enable the training of very deep networks [63].

In Natural Language Processing (NLP) tasks, feedback mechanisms such as attention and recurrent structures help the network understand context and generate coherent text. For instance, attention mechanisms in machine translation focus on relevant parts of the source sentence while generating the target sentence, thereby improving translation quality [56]. Recurrent Neural Networks (RNNs) and other feedback mechanisms model temporal dependencies in time series analysis, making predictions based on past observations. This is crucial for applications like stock price prediction, weather forecasting, and anomaly detection in sensor data [64].

It is essential to understand the training processes that enable neural networks to learn from data to build on these varied applications of feedback mechanisms. This involves exploring different learning paradigms, such as supervised and unsupervised learning.

## Learning Paradigms

Neural networks can be trained using different learning paradigms, with supervised and unsupervised learning being the most common.

### *Supervised Learning*

Supervised learning, as shown in Fig. 3.11 [65], involves training a neural network on a labeled dataset, where each training example consists of an input and a corresponding target output. The network learns to map inputs to outputs by adjusting its weights to minimize the prediction error. This iterative learning process requires substantial labeled data to achieve high accuracy [48].

Collecting and preparing data is crucial in supervised learning. The dataset must include many labeled examples that are accurately annotated to train the network effectively. The quality and quantity of the data directly impact the network's performance [66]. During training, the network processes input data through layers, applies activation functions, and generates predictions. The error between the predicted and actual outputs is computed using a loss

function. This error is then propagated backward through the network (backpropagation), and the weights are updated using an optimization algorithm like gradient descent to reduce the error [42].

To ensure the model generalizes well to new data, a separate validation set (typically 80% training: 20% test) is used during training to monitor performance and prevent overfitting. After training, the model is tested to assess its accuracy, generalizability, and production readiness [67]. Supervised learning is widely used in various applications, such as image classification, speech recognition, and natural language processing. For instance, in image classification, the network is trained on labeled images and learns to predict the category of new images. In speech recognition, the network converts spoken language into text by learning from audio recordings and their transcriptions [68].

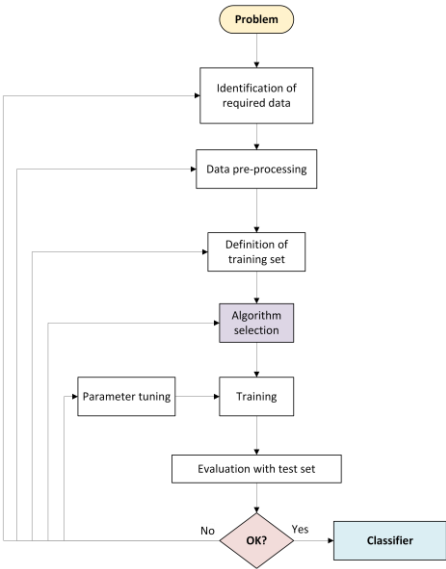


Figure 3.11: Supervised Learning Process Flow [65]

## *Unsupervised Learning*

In unsupervised learning, the network learns from unlabeled data, where the goal is to identify patterns and structures without explicit target outputs. This paradigm is useful for exploratory data analysis and discovering hidden structures in data [69].

Clustering algorithms group similar data points based on their features. Neural networks, such as autoencoders and deep clustering models, can learn to represent data in a lower-dimensional space and identify clusters. This technique is useful in applications like market segmentation and biological

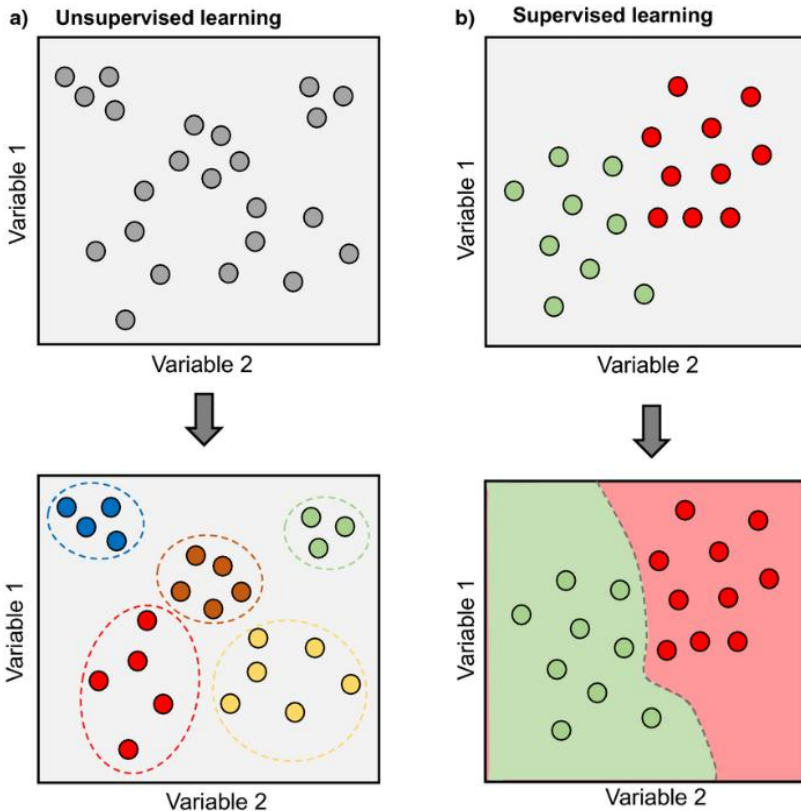


Figure 3.12: Comparison of Supervised and Unsupervised Learning [71]

data analysis, where the objective is to group similar entities [70]. A comparison of supervised and unsupervised learning can be seen in Fig. 3.12 [71].

Techniques like Principal Component Analysis (PCA) and t-Distributed Stochastic Neighbor Embedding (t-SNE) reduces the number of variables under consideration while preserving the essential structure of the data. Neural networks like autoencoders can also minimize dimensionality by learning compact data representations. This is beneficial for data visualization and noise reduction [72].

Unsupervised learning is also used to detect anomalies or outliers in data. For example, neural networks can analyze traffic in network security to identify unusual patterns indicating cyber-attacks. In manufacturing, anomaly detection helps identify product defects by recognizing deviations from normal patterns [73].

### ***Semi-Supervised Learning***

Semi-supervised learning combines a small amount of labeled data with a large amount of unlabeled data during training. This approach is useful when labeling data is expensive or time-consuming. Neural networks can leverage unlabeled data to learn underlying structures and improve performance on the labeled data [74].

The network is initially trained on the labeled data and then uses the learned features to predict the unlabeled data. These predictions are refined iteratively, improving the model's accuracy. Semi-supervised learning bridges the gap between supervised and unsupervised learning, making efficient use of both labeled and unlabeled data [75]. Semi-supervised learning is used in various fields, such as text classification, image recognition, and bioinformatics. For example, in text classification, a small set of labeled documents can be used to train the network, predicting the categories of a larger set of unlabeled documents.

### ***Reinforcement Learning***

Reinforcement learning involves training an agent to make decisions by acting in an environment to maximize cumulative rewards. The agent learns from

feedback through rewards or penalties and adjusts its actions based on this feedback [76].

The agent interacts with the environment, observes the outcomes of its actions, and receives rewards or penalties. It uses this information to update its policy, a strategy for choosing actions. Over time, the agent learns to maximize its cumulative rewards by refining its policy [77]. Reinforcement learning is used in robotics, game-playing, and autonomous systems. For example, in robotics, an agent learns to perform tasks through trial and error, such as navigating a maze or manipulating objects. In-game playing, reinforcement learning algorithms, such as those used in AlphaGo, have achieved superhuman performance in complex games by learning optimal strategies through extensive self-play [44].

Having explored the various learning paradigms, it is essential to understand how neural networks can mimic certain aspects of human intelligence and recognize complex patterns, which will be covered in the following sections.

### ***Mimicking Human Intelligence***

Neural networks can mimic certain aspects of human intelligence, such as pattern recognition, language understanding, and decision-making. However, they do so in a fundamentally different way from the human brain. Neural networks operate based on mathematical computations and statistical learning, whereas human intelligence involves consciousness, emotions, and understanding [78]. A comparison can be found in the table below.

Neural networks are designed to solve specific tasks by learning from data. They excel at tasks that require pattern recognition and prediction, such as image and speech recognition, language translation, and game playing. However, neural networks lack the general intelligence and adaptability of the human brain. They are limited to the tasks they are trained on and do not possess the ability to understand or reason beyond their training. This distinction highlights the difference between narrow AI, where neural networks excel, and Artificial General Intelligence (AGI), which remains an unsolved challenge in the field [61]. For further understanding, table 2.1 [79] compares ANN and Natural Neural Networks, our brain. Now that you have a

sense of function, architecture, and the types of Neural Networks, let’s explore some real-world examples to strengthen your understanding of the topic.

Table 2.1: Artificial Neural Networks vs Biological Neural Networks [76]

Characteristics	Artificial Neural Network (ANN)	Biological Neural Network (BNN)
Speed	Faster in processing information. Response time is in nanoseconds.	Slower in processing information. The response time is in milliseconds.
Processing	Serial processing.	Massively parallel processing.
Size & Complexity	Less size & complexity. It does not perform complex pattern recognition tasks.	A highly complex and dense network of interconnected neurons containing neurons of the order of $10^{11}$ with $10^{15}$ interconnections.
Number of Neurons	Varies based on design, typically in the range of thousands to millions.	Approximately $10^{11}$ (100 billion) neurons.
Storage	Information storage is replaceable, meaning replacing new data with old data.	Information storage is adaptable, adding new information by adjusting the interconnection strengths without destroying old information.

<b>Fault Tolerance</b>	Fault intolerant. Corrupt information cannot be retrieved in case of system failure.	Fault-tolerant. Information storage is adaptable, adding new information by adjusting the interconnection strengths without destroying old information.
<b>Control Mechanism</b>	There is a control unit for controlling computing activities.	There is no specific control mechanism external to the computing task.

# Real-World Example Solving Real-World Problems

One of the most profound applications of neural networks is healthcare, specifically in diagnosing diseases through medical imaging, as shown in Fig. 3.13 [80]. The traditional process of diagnosing diseases like cancer from medical images such as mammograms or CT scans is time-consuming and requires highly skilled radiologists. Even then, human analysis is subject to

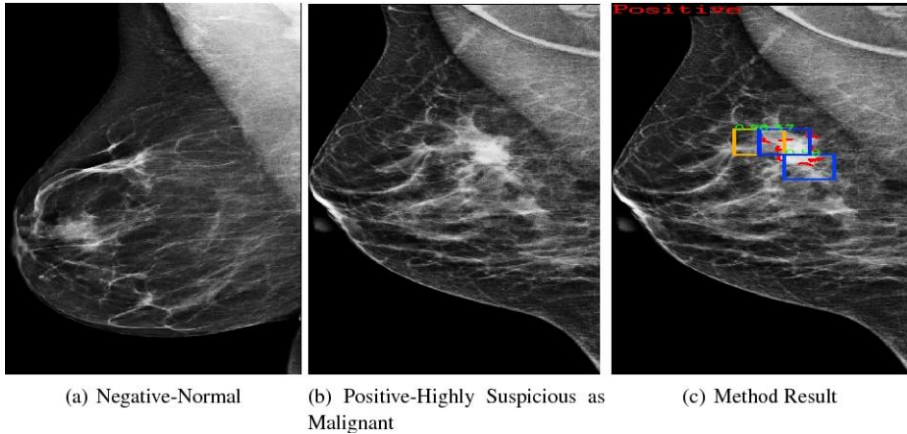


Figure 3.13: Mammogram Image [80]

variability and error. This is where neural networks, particularly deep learning models, have shown transformative potential [81].

Breast cancer is one of the leading causes of cancer-related deaths among women worldwide. Early detection significantly improves the chances of successful treatment and survival. However, interpreting mammograms to detect early signs of cancer is challenging due to the subtle differences between benign and malignant tissues [82].

CNNs are designed to automatically and adaptively learn spatial hierarchies of features from input images. Large datasets of mammogram images are collected and annotated by expert radiologists. The CNN model is trained using these labeled images to recognize patterns and features that differentiate normal tissues from cancerous ones. Once trained, CNNs can analyze new, unseen mammogram images to predict the likelihood of cancer, assisting radiologists in making more accurate and faster diagnoses [83]. Fig. 3.14 [84] shows the inputs, channels, activation, and convolutional neural network that allow for this type of detection of patterns and learning.

In addition to breast cancer detection, neural networks have significantly impacted the diagnosis of brain disorders through advanced imaging techniques. Early detection and accurate diagnosis are crucial in treating brain disorders such as Alzheimer's disease, brain tumors, and stroke. The ability of

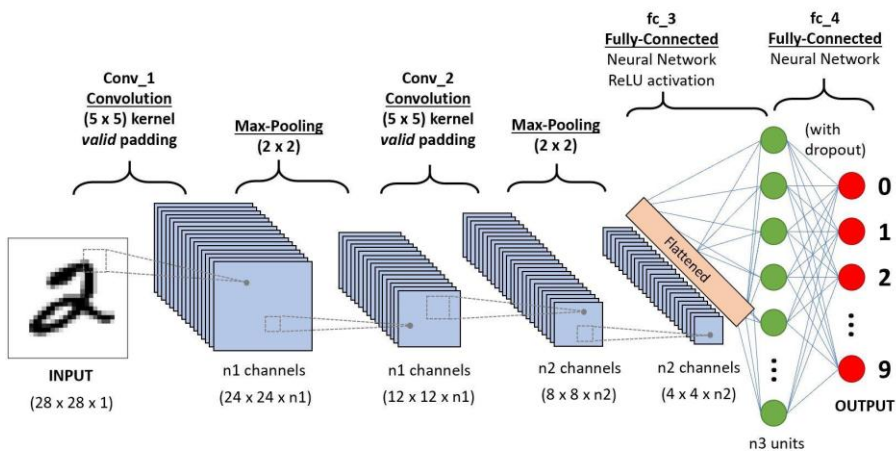


Figure 3.14: Convolutional Neural Network Architecture [84]

neural networks to analyze and interpret complex brain images offers substantial improvements over traditional methods, which are often time-consuming and prone to variability.

Convolutional Neural Networks (CNNs) have been extensively used in brain imaging due to their proficiency in processing grid-like data structures such as MRI scans, as shown in Fig. 3.15 [85]. A prominent application of CNNs in brain imaging is the early detection of Alzheimer's disease. Alzheimer's disease is a progressive neurodegenerative disorder characterized by the accumulation of amyloid plaques and tau tangles in the brain, leading to cognitive decline and memory loss. Early detection is critical as it can significantly improve treatment effectiveness and slow the disease's progression. In the early detection of Alzheimer's disease, large datasets of MRI scans are collected from patients diagnosed with the disease and healthy controls. Medical experts annotate these images to identify brain regions affected by Alzheimer's. The CNN model is then trained using these labeled images to learn the distinguishing features of Alzheimer's disease. The network's layers automatically extract relevant features from the input images, such as differences in brain volume and the presence of amyloid plaques.

During training, CNN learns to recognize patterns in MRI scans indicative of Alzheimer's disease. The network adjusts its weights through backpropagation and gradient descent to minimize the prediction error. This iterative process involves multiple epochs, where the network repeatedly processes the training data and refines its predictions. Data augmentation, regularization, and

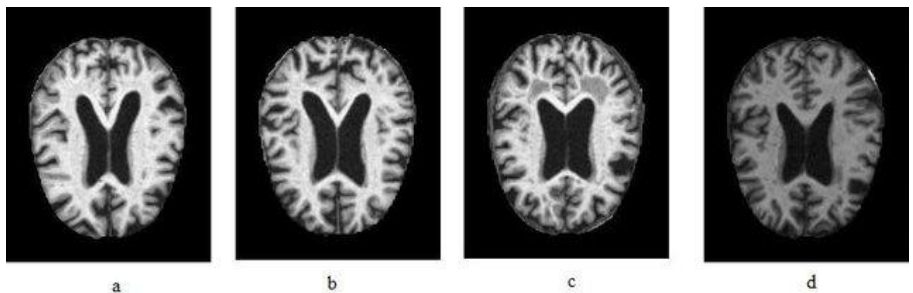


Figure 3.15: MRI images of (a) Mild Demented, (b) Moderate Demented, (c) Non-Demented, and (d) Very Mild Demented. Though the images may seem meaningless, a CNN identified the correct Alzheimer's stage with a >95% accuracy [85]

dropout enhance the training process and prevent overfitting, ensuring the model generalizes well to new, unseen data.

Once trained, CNNs can analyze new MRI scans to predict the likelihood of Alzheimer's disease. The network's predictions assist radiologists in making more accurate and timely diagnoses. Studies have shown that CNNs can achieve high sensitivity and specificity in detecting Alzheimer's, often outperforming traditional diagnostic methods. For instance, a study by Abdul Azeem et al. (2021) demonstrated that a CNN-based model could classify Alzheimer's disease with an accuracy of over 97%, highlighting the potential of deep learning in clinical practice.

Recent advancements in neural network techniques have significantly improved the early diagnosis and classification of Alzheimer's disease. For example, a hybrid deep learning approach combining BiLSTM and ANN models has shown promise in early diagnosis by capturing long-range dependencies and temporal dynamics within medical records [86].

Additionally, a novel multi-scale attention-based pseudo-3D convolutional neural network has been developed for Alzheimer's diagnosis using structural MRI data. This method leverages attention mechanisms to focus on critical features, enhancing the network's ability to classify different stages of Alzheimer's disease accurately.

Another innovative approach involves using a deeply supervised adaptable neural network that integrates multitask feature extraction for diagnosing and classifying the severity of Alzheimer's disease. This method utilizes traditional machine learning techniques and deep learning models to analyze MRI images, comprehensively assessing Alzheimer's severity [87].

These applications of neural networks in brain imaging underscore their transformative potential in healthcare. By leveraging advanced machine learning techniques, neural networks provide potent tools for early detection, accurate diagnosis, and effective treatment planning for brain disorders. As research progresses, integrating neural networks with medical imaging is expected to yield even more sophisticated diagnostic capabilities, ultimately enhancing patient care and outcomes.

# Ethical, Privacy, and Security

## *Considerations in Neural Network Development*

As neural networks become more prevalent, ethical, privacy, and security considerations in their development and deployment are increasingly important. Neuroengineering students must be aware of these issues to ensure the responsible use of this technology.

One significant concern is bias and fairness. Neural networks can inadvertently learn and perpetuate biases in the training data, leading to unfair or discriminatory outcomes. For example, a facial recognition system trained on a dataset with limited diversity may perform poorly on specific demographic groups. Addressing bias and ensuring fairness involves collecting diverse and representative datasets, developing techniques to detect and mitigate bias, and providing transparency and accountability in model development [88].

Think about a wearable that was trained to look at skin cancer. The skin training data set may be primarily Caucasians due to the location of the clinical trials and the focus on diversity. This poses a significant setback in the ability of the device to detect skin cancer in those with darker pigments, rendering the device ineffective in many regions of the world. Privacy is another critical issue.

Neural networks often require vast amounts of data to achieve high performance, including sensitive personal information such as medical records, financial transactions, and social media activity. Ensuring data privacy is crucial to protect individuals' rights and maintain public trust. Data anonymization, differential privacy, and federated learning are being developed to enable neural networks to learn from data without compromising individual privacy [89], [90].

In addition to privacy, security is a significant concern. Neural networks are vulnerable to adversarial attacks, where malicious inputs are crafted to deceive the network into making incorrect predictions. These attacks can have serious consequences, especially in critical applications such as autonomous vehicles, healthcare, and security systems. Developing robust neural networks that can withstand adversarial attacks is an active area of research [91].

Ethical AI guidelines play a crucial role in addressing these concerns. Developing and adhering to such guidelines is essential for responsible neural network development. Like that of Fig. 3.16 [92], ethical frameworks should emphasize fairness, transparency, accountability, and privacy. Compliance with relevant laws and regulations and engaging with diverse stakeholders are crucial to ensure ethical AI development [93]. Addressing the ethical considerations in neural network development involves mitigating biases, protecting privacy, providing security, and adhering to ethical guidelines to foster transparency, accountability, and fairness in AI systems. These all contribute to what the future of AI and Neural Networks will look like.



Figure 3.16: Ethical AI Framework from [92]

## **Future Directions and Challenges**

The field of neural networks is rapidly evolving, with ongoing research addressing current challenges and exploring new frontiers.

Researchers continually develop new neural network architectures to improve performance and expand capabilities. Transformer networks, for example, have revolutionized natural language processing with their self-attention mechanisms [56]. Graph neural networks (GNNs) are designed to process graph-structured data, such as social networks and molecular structures [94]. Spiking neural networks (SNNs) aim to mimic biological neurons' asynchronous and event-driven nature, potentially leading to more efficient and biologically plausible models [95].

### ***Interdisciplinary Research***

The intersection of neural networks with other fields, such as neuroscience, biology, and physics, offers exciting opportunities for interdisciplinary research. Collaborations between AI researchers and neuroscientists are leading to a deeper understanding of brain function and the development of biologically inspired neural networks. In biology and medicine, neural networks are used to analyze biological data, model biological processes, and develop personalized medicine approaches. Quantum neural networks (QNNs) are an emerging field exploring the potential of quantum computing to perform computations that are infeasible for classical computers [96].

### ***Ethical and Societal Impact***

As neural networks become more integrated into society, addressing their ethical and societal impact remains a critical challenge. Ensuring ethical AI development involves ongoing research into bias mitigation, fairness, and transparency. Understanding the societal implications of AI, such as its impact on employment, privacy, and security, is essential for responsible AI deployment. Developing policies and governance frameworks to regulate AI development and use is crucial for ensuring that AI benefits society as a whole [93].

## *Recent Advances and Future Directions*

1. **Neural Architecture Search (NAS):** Automated methods for designing neural network architectures are gaining traction. NAS techniques aim to identify optimal architectures for specific tasks, potentially outperforming human-designed models [97].
2. **Federated Learning:** This approach trains models across decentralized devices while preserving data privacy. Federated learning is particularly relevant for applications involving sensitive data, such as healthcare [98].
3. **Explainable AI (XAI):** As AI systems become more complex, it is crucial to ensure their transparency and interpretability. XAI research focuses on developing methods to make neural network decisions understandable to humans [99].
4. **AI and Climate Change:** Neural networks model climate systems and predict environmental changes. This research is vital for developing strategies to mitigate the impact of climate change [100].
5. **Advanced Reinforcement Learning:** Techniques such as meta-reinforcement learning and hierarchical reinforcement learning are expanding the capabilities of AI systems to learn complex tasks efficiently [101].
6. **Neuromorphic Computing:** Inspired by the human brain, neuromorphic computing aims to develop hardware that mimics neural architectures, potentially leading to more efficient and powerful AI systems [102].

As we conclude this chapter, we've explored the transformative power of neural networks and their profound impact on various fields. From their historical evolution and fundamental workings to the diverse types and real-world applications, neural networks have demonstrated their capability to solve complex problems. Ethical, privacy, and security considerations are paramount in their development, ensuring responsible and fair use. The future holds exciting advancements in architecture and interdisciplinary research, promising to enhance further the capabilities and applications of neural networks, ultimately benefiting society as a whole. As you move forward,

consider these key aspects and their implications in the broader context of artificial intelligence and neurotechnology.

## **Chapter 3: Summary**

In this chapter, we have systematically examined the core principles and practical applications of neural networks. We began by detailing the fundamental architecture of neural networks, including the roles of neurons, layers, and activation functions, which collectively enable these systems to process and learn from data. This foundation was further contextualized by tracing the historical development of neural networks, highlighting key innovations that have driven their current capabilities, particularly in deep learning.

We then explored various types of neural networks, each designed to address specific computational tasks. Convolutional Neural Networks (CNNs) were shown to excel in image processing, while Recurrent Neural Networks (RNNs) demonstrated their utility in handling sequential data. These architectures have been instrumental in advancing fields such as healthcare, where neural networks are now critical in tasks like disease diagnosis and treatment planning.

Ethical considerations were also addressed, emphasizing the importance of mitigating bias, safeguarding privacy, and enhancing security in developing and deploying neural networks. As these technologies become more integrated into critical applications, it is essential to create robust frameworks to ensure responsible use.

Looking forward, the field of neural networks is poised for continued advancement. Ongoing research into new architectures and interdisciplinary approaches will likely yield further performance improvements and expand these systems' applicability. However, with these developments comes the responsibility to manage the societal impacts of neural networks, ensuring that their deployment is ethical and beneficial to various stakeholders.

In the coming chapters, we will focus on neuroengineering technologies such as EEG, fMRI, and Brain-Computer Interfaces (BCI). These tools are essential for understanding and treating neurological diseases and offer new avenues for interfacing directly with the human brain. As we delve into these technologies and their applications, we will continue to build on the foundation laid by our

exploration of neural networks, connecting these advances to the broader field of neurotechnology.

This chapter has provided a comprehensive overview of neural networks, grounding your understanding in their theoretical underpinnings and practical applications. As you move deeper into the study of artificial intelligence and neurotechnology, the knowledge gained here will serve as a critical foundation for understanding and developing future innovations in these fields.



## Chapter 3: Learning activities

### Learning Activity 3.1

Using the Buzz groups technique, propose the following challenge as the students to give an example of how you are using NN today. Also, this classroom assumes the student is working on a semester-long engineering project; how would you use them in your project?



---

### Learning Activity 3.2

A quescussion, a blend of "question" and "discussion," is an interactive and participatory teaching and learning technique where participants engage in a dialogue of questions. This method stimulates critical thinking, active participation, and deeper topic exploration. The rules of a quescussion are simple: participants can only contribute by asking questions, not by making statements or providing answers.



Key Features of a Quesession:

- **Question-Only Dialogue:** Participants can only speak in the form of questions, avoiding statements, answers, or declarative comments.
- **Open-Ended Questions:** Questions are typically open-ended to promote thought, reflection, and further inquiry.
- **Group Participation:** All participants are encouraged to contribute questions, fostering an inclusive and engaging environment.
- **Facilitation:** A facilitator may guide the process, ensuring the discussion remains focused and productive while maintaining the question-only rule.
- **Reflective Learning:** The format encourages participants to think deeply and consider multiple perspectives, enhancing critical thinking and understanding.

Example: Here's an example of a quesdiscussion on the topic of "Artificial Intelligence in Education":

Facilitator: "Let's begin our quesdiscussion on the impact of artificial intelligence (AI) in education. Remember, you can only ask questions; no statements or answers are allowed. Who wants to start?"

Participant 1: "How is AI currently being used in classrooms?"

Participant 2: "What are the potential benefits of AI for personalized learning?"

Participant 3: "Could AI help teachers with administrative tasks?"

Participant 4: "What are the risks associated with relying on AI for grading and assessments?"

Participant 5: "How might AI affect the role of teachers in the future?"

Participant 6: "Are there ethical considerations we must address when implementing AI in education?"

Participant 7: "What are some examples of successful AI tools already used in education?"

Participant 8: "How can we ensure AI is accessible to all students, regardless of their socio-economic background?"

Participant 9: "What training do teachers need to use AI effectively?"

Participant 10: "How can AI help identify and support students with learning difficulties?"

Participant 11: "What are the long-term impacts of AI on student privacy?"

Participant 12: "How do students feel about interacting with AI in their learning environments?"

Facilitator: "Great set of questions! Let's keep going. Who has the next question?"

Participant 13: "What kind of data does AI need to personalize learning experiences?"

Participant 14: "Can AI adapt to different learning styles and paces?"

Participant 15: "How do we measure the effectiveness of AI in education?"

This format encourages continuous inquiry and exploration of the topic, allowing participants to dive deeper into the subject matter through a series of interconnected questions.

Following this technique, propose the following quescussion; start with the bold statement: “Unsupervised learning is better than supervised learning.”

---

## Learning Activity 3.3

The following website provides an easy way to demonstrate how machine learning works. By following these simple steps, students can learn and apply the concepts:

1. Collect examples of the items you want the system to recognize.
2. Train a computer using these examples to recognize the items.
3. Create a game in Scratch that leverages the computer's recognition capabilities.

Have your students apply this procedure to pattern recognition in a neuroengineering-related process, allowing them to select which aspect they want to classify.

Game: <https://machinelearningforkids.co.uk/>



## Chapter 3: Lab introduction

In this series of lab exercises, you will introduce the world of neural networks and their diverse applications, ranging from general machine learning tasks to specialized neuroengineering projects. These labs will provide practical experience in developing, training, and evaluating neural networks, enhancing your understanding of their functionality and potential applications.

You will start by exploring the fundamental concepts of neural networks, which are inspired by the structure and functioning of the human brain. These powerful tools can learn from data and make intelligent decisions, proving essential in fields such as image recognition, natural language processing, and neuroengineering. Through hands-on activities, you will gain insights into how neural networks are structured and how they operate.

Next, using a fictional dataset, you will apply your knowledge by developing a neural network to predict injury risk from vehicle crash data. This exercise will involve generating sample data, building and training the neural network, and testing its performance with input data to evaluate its functionality. By the end of these labs, you will have practical experience applying neural networks to research datasets, preparing you for further exploration in machine learning and neuroengineering.



# Chapter 3: Lab Example 1



## *Introduction*

This practical lab example will explore the fascinating world of neural networks and their applications in general machine learning and specialized neuroengineering tasks. Neural networks, inspired by the structure and functioning of the human brain, are powerful tools capable of learning from data and making intelligent decisions. They have become essential in various fields, from image recognition and natural language processing to more advanced applications like neuroengineering.

First, we will start with a simple yet classic example of using neural networks: training a model to recognize handwritten digits from the MNIST dataset. This example introduces fundamental concepts and provides hands-on experience in building, training, and evaluating a neural network using TensorFlow and Keras. The MNIST dataset, comprising 70,000 images of handwritten digits, is a standard benchmark for evaluating image classification algorithms.

Following this introductory example, we will delve into a more advanced and specialized application in the field of neuroengineering: training a neural network to recognize artifacts in MRI images. MRI artifacts can obscure the quality of scans and hinder accurate diagnosis and treatment planning. By training a neural network to identify and correct these artifacts, we can enhance the precision of neuroimaging techniques, ultimately improving patient outcomes.

This lab will guide you through downloading the necessary tools, preprocessing data, building neural network models, and training and evaluating these models on specific datasets. Whether new to neural networks or looking to expand your knowledge into neuroengineering applications, these examples will provide a solid foundation and practical skills to apply in future projects.

## *Example 1: MNIST Handwriting Training*

To avoid any library or Python environment dependencies, we will use Google Collaboratory. Type it into Google and sign up for free with a Gmail account.

Like with a Jupiter Notebook, you will be well on your way to training and testing a neural network.

### ***Step 1: Install Required Libraries***

First, you must install TensorFlow (if you are using your local machine or if Colab errors arise). You can do this using pip:

```
pip install tensorflow
```

### ***Step 2: Import Libraries***

Next, we need to import the necessary libraries in our Python script:

```
Import tensorflow as tf
from tensorflow.keras.datasets import mnist
from tensorflow.keras.models import Sequential
from tensorflow.keras.layers import Dense, Flatten
from tensorflow.keras.utils import to_categorical
```

### ***Step 3: Load and Preprocess the Data***

We will load the MNIST dataset and preprocess it for our neural network:

```
# Load the MNIST dataset
(x_train, y_train), (x_test, y_test) =
mnist.load_data()

# Normalize the input data
x_train = x_train.astype('float32') / 255
x_test = x_test.astype('float32') / 255

# Convert labels to categorical one-hot encoding
y_train = to_categorical(y_train, 10)
y_test = to_categorical(y_test, 10)
```

### ***Step 4: Build the Neural Network Model***

We will build a simple neural network model:

```
# Initialize the model
model = Sequential()

# Add layers to the model
model.add(Flatten(input_shape=(28, 28))) # Flatten
the input shape (28x28 pixels)
model.add(Dense(128, activation='relu')) # Add a
fully connected layer with 128 units and ReLU
activation
model.add(Dense(10, activation='softmax')) # Add a
fully connected layer with 10 units (one for each
class) and softmax activation

# Compile the model
model.compile(optimizer='adam',
loss='categorical_crossentropy', met-
rics=['accuracy'])
```

### ***Step 5: Train the Model***

We will train the model using the training data:

```
# Train the model
model.fit(x_train, y_train, epochs=5,
batch_size=32, validation_split=0.2)
```

### ***Step 6: Evaluate the Model***

Finally, we will evaluate the model using the test data:

```
# Evaluate the model
test_loss, test_accuracy = model.evaluate(x_test,
y_test)
print(f'Test loss: {test_loss}')
print(f'Test accuracy: {test_accuracy}')
```

```

Downloading data from https://storage.googleapis.com/tensorflow/tf-keras-datasets/mnist.npz
11490434/11490434 [=====] - 0s 0us/step
Epoch 1/5
1500/1500 [=====] - 8s 5ms/step - loss: 0.2919 - accuracy: 0.9160 - val_loss: 0.1622 - val_accuracy: 0.9539
Epoch 2/5
1500/1500 [=====] - 5s 3ms/step - loss: 0.1295 - accuracy: 0.9621 - val_loss: 0.1149 - val_accuracy: 0.9642
Epoch 3/5
1500/1500 [=====] - 7s 5ms/step - loss: 0.0878 - accuracy: 0.9737 - val_loss: 0.1011 - val_accuracy: 0.9693
Epoch 4/5
1500/1500 [=====] - 5s 3ms/step - loss: 0.0648 - accuracy: 0.9799 - val_loss: 0.0963 - val_accuracy: 0.9709
Epoch 5/5
1500/1500 [=====] - 7s 5ms/step - loss: 0.0500 - accuracy: 0.9850 - val_loss: 0.0886 - val_accuracy: 0.9732
313/313 [=====] - 1s 2ms/step - loss: 0.0865 - accuracy: 0.9748
Test loss: 0.08651327341794968
Test accuracy: 0.974799906539917

```

Figure 3.17: Evaluating the model

It doesn't look fancy, but you have trained and tested a Neural Network (Fig. 3.17).

Let's do something a little more challenging to continue on this track. Let's train a model to recognize certain artifacts or features in brain MRI images with MRI\_Visualization.py.

**NOTE: This code should be used in Google Colab (free) or Jupyter notebook by placing the code in code cells within the notebook.**

We will start with loading the data, processing it, Training, & Testing, and then we can start with some ML Predictions based on the inputted data.

```

# Define the path to the participant data file in your Google
Drive
participant_data_path = '/content/drive/MyDrive/Brain-MRI-
Age-Classification-using-Deep-Learning/ds000228-1.1.0-sub-
set/derivatives/participants.tsv'

# Load participant data
participant_data = pd.read_csv(participant_data_path,
sep='\t')
participant_data['AgeClass'] = pd.cut(partici-
pant_data['Age'], bins=[3, 6, 13, np.inf], labels=['Ages3-
5', 'Ages7-12', 'Adults'])

# Display the first few rows of the participant data
participant_data.head()

```

	participant_id	Age	AgeGroup	child_adult	Gender	Handedness	ToM Booklet-Matched	ToM Booklet-Matched-NOFB	FB_composite	FB_group	WPPSI BD raw	WPPSI BD scaled	KBIT_raw	KBIT_standard	DCIS summary	Scanlog: scanner
0	sub-pixar001	4.774812	4yo	child	M	R	0.80	0.736842	6.0	pass	22.0	13.0	NaN	NaN	3.0	3T1
1	sub-pixar002	4.856947	4yo	child	F	R	0.72	0.736842	4.0	inc	18.0	9.0	NaN	NaN	2.0	3T1
2	sub-pixar003	4.153320	4yo	child	F	R	0.44	0.421053	3.0	inc	15.0	9.0	NaN	NaN	3.0	3T1
3	sub-pixar004	4.473648	4yo	child	F	R	0.64	0.736842	2.0	fail	17.0	10.0	NaN	NaN	3.0	3T1
4	sub-pixar005	4.837782	4yo	child	F	R	0.60	0.578947	4.0	inc	13.0	5.0	NaN	NaN	2.0	3T1

Figure 3.18: Data Structure

The structure of the data is shown in Fig. 3.18; we won't share images of the epochs and training, but in Fig. 3.19, you will see the output of a convolution matrix, predictions, and Occlusion Maps of the images of the brain.

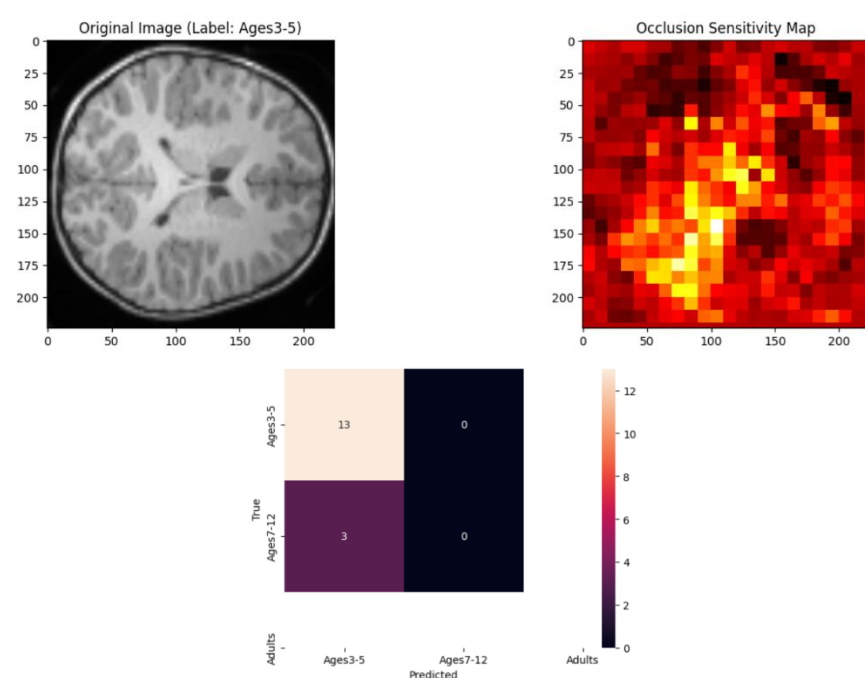


Figure 3.19: Output of convolution matrix, predictions and Occlusion maps



# Chapter 3: Lab Example 2

## Introduction

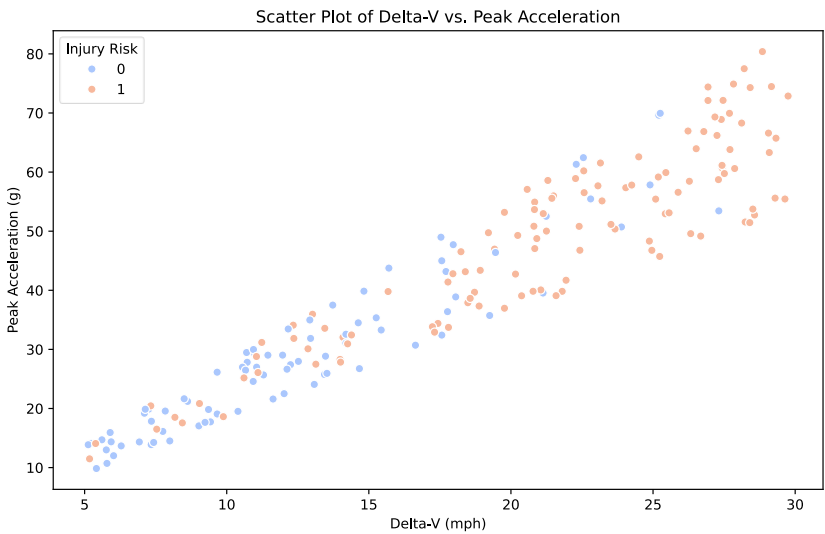
In this lab example, we will develop our neural network (NN) to predict injury risk from vehicle crash data using artificial data to illustrate how you could apply NNs to your research. We will generate sample data, build and train the NN, and then test it with input data to evaluate its functionality. To reiterate, this is an entirely fictional dataset meant to illustrate the application of NNs to various research datasets.



## Exercise Instructions

### Step 1: Generate Sample Data

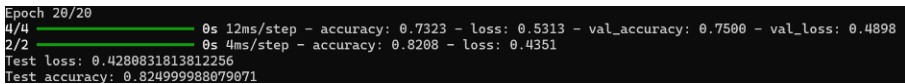
First, we will generate synthetic data to simulate vehicle crash database information. Imagine this data could be any form of information, whether training for images as shown in Fig. 3.20 or a large dataset with a range of



variables as in this example. Obviously, the type of network you design will change, but this is meant to be a very basic exercise. We will include vehicle type, crash severity, peak acceleration, and corresponding injury risk for this artificially generated data. See the GitHub for the complete code. For now, our generated data is artificially skewed with some variability and noise to introduce realistic trends in data to improve this theoretical model's prediction accuracy (increased severity leads to increased injury risk) while attempting to include some degree of variability. This is a scatter plot of what our generated dataset looks like:

### ***Step 2: Write and execute the neural network training script***

Write and execute the training script for the neural network code using the code in GitHub. You can see the Keras model is being used here. Additionally, some of the data is normalized within this code as well. As you learned in this chapter, normalization is a key step to ensure that each feature contributes proportionately to the model's learning process. After executing the training script, we see the following:



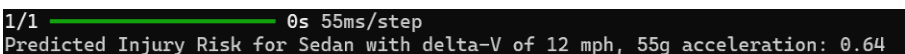
```
Epoch 20/20
4/4 ————— 0s 12ms/step - accuracy: 0.7323 - loss: 0.5313 - val_accuracy: 0.7500 - val_loss: 0.4898
2/2 ————— 0s 4ms/step - accuracy: 0.8208 - loss: 0.4351
Test loss: 0.4280831813812256
Test accuracy: 0.824999988079671
```

Figure 3.21: Network Training

As you can see in this screenshot, the model completed 20 epochs, and the test loss was 0.4281 with an accuracy of 82.5%. This effectively accomplishes the goal of training a custom neural network from a dataset. We could take this further by predicting the injury risk from the provided data.

### ***Step 3: Write and execute prediction code***

Let's re-load the neural network while also having it predict injury risk from a sedan with a 12mph delta-V (collision severity) and 55g peak acceleration. The following output is observed after the model is re-trained:



```
1/1 ————— 0s 55ms/step
Predicted Injury Risk for Sedan with delta-V of 12 mph, 55g acceleration: 0.64
```

Figure 3.22: Prediction Output

## *Discussion*

Based on the trained data, the neural network predicts the injury risk from our sedan of 12mph dV and 55g acceleration to be 64%. This could be likened to the typical logistic regression type analysis typically conducted for these types of datasets. However, even in this simple feed-forward type of neural network we generated, it is clear how many variables could be included to train the network, including non-linear or variable data. Unlike logistic regression, neural networks can handle non-linear relationships and complex patterns in the data. There can be overfitting concerns and various other considerations already discussed in the chapter. This laboratory example shows a simplistic method for training a feedforward neural network for classification tasks.





## **Chapter 4**

# **Brainwaves Unleashed: EEG and MEG**

# Introduction and Learning Objectives

In this chapter, we will explore the critical role of Electroencephalography (EEG) and Magnetoencephalography (MEG) in neuroengineering. These non-invasive techniques are essential for recording and analyzing the brain's electrical and magnetic activities. The chapter will provide a comprehensive understanding of the operational principles, hardware, and setup of EEG and MEG systems, as well as their applications and significance. By the end of this chapter, you will be able to

1. *Recognize the functional significance of EEG frequency bands and their association with cognitive states.*
2. *Understand the setup and configuration procedures for accurate data acquisition.*
3. *Describe the components and technical specifications of EEG and MEG systems.*
4. *Explain the operational principles of MEG and its components.*
5. *Identify noise sources in EEG and MEG recordings and strategies for minimizing them.*
6. *Explain the software tools used for EEG and MEG studies' signal processing and data analysis.*

Understanding the historical development of EEG and MEG can provide valuable context. EEG, first developed by Hans Berger in the 1920s, revolutionized brain research by allowing scientists to record electrical activity from the scalp. MEG, however, was introduced in the late 1960s and 1970s thanks to advancements in superconducting technology. Both technologies have evolved significantly, with EEG widely used in clinical and research settings and MEG providing unparalleled precision in mapping brain activity. This historical perspective shows how technological advancements have continually improved our ability to study the brain.

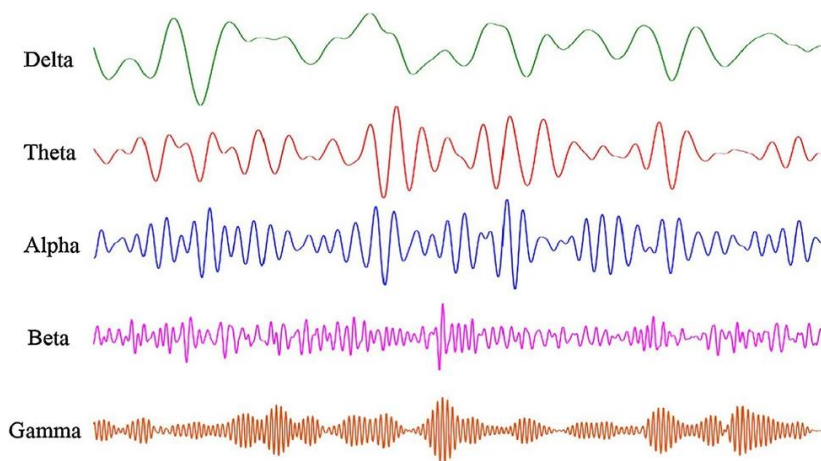


Figure 4.1: EEG Frequency Band Classifications [104]

## Classification of EEG

Electroencephalography (EEG) is a noninvasive method for recording electrical activity in the brain. This technique is crucial in neuroengineering as it helps us understand various brain functions and states. EEG signals are classified by the frequency bands of the brain waves they capture. These frequency bands, Delta, Theta, Alpha, Beta, and Gamma, represent different types of neural activity and cognitive states [103].

### *EEG Frequency Bands: Delta, Theta, Alpha, Beta, Gamma*

EEG frequency bands are categorized based on their oscillation rates, measured in Hertz (Hz). Table 4.1 shows the different band types and associated brain functions. Fig. 4.1 [104] illustrates the different EEG frequency bands, showcasing the distinct waveforms related to Delta, Theta, Alpha, Beta, and Gamma bands over a five-second interval [103].

Table 4.1: Band Types

Band	F(Hz)	Frequency Description	Function
Delta	0.5-4	Delta waves are the slowest and are typically observed during deep sleep. They play a role in restorative processes within the body and brain.	Essential for restorative sleep and healing processes, delta waves facilitate deep restorative sleep and are crucial for physical and mental recovery.
Theta	4-8	Theta waves are prevalent during light sleep, deep meditation, and relaxation.	Linked with memory and learning, theta waves emerge during light sleep and deep meditation, facilitating memory consolidation and creative thinking.
Alpha	8-13	Alpha waves are dominant when awake but relaxed, often with closed eyes.	Associated with relaxation and stress reduction, alpha waves dominate during restful, wakeful states and indicate a calm and meditative mind.
Beta	13-30	Beta waves are faster and are seen during active thinking, problem-solving, and focused mental activity.	Representing active concentration and problem-solving, beta waves are prominent during tasks requiring focused mental effort and active thinking.
Gamma	30-100	Gamma waves are the fastest and are associated with high-level information processing, including perception, consciousness, and cognitive functioning.	Associated with peak cognitive functioning and information processing, gamma waves are involved in tasks requiring high-level cognitive functions, such as problem-solving, perception, and consciousness.

***Analytical Techniques: Band Power, Connectivity Analysis***

To extract meaningful information from EEG data, several analytical techniques are employed:

**Band Power**

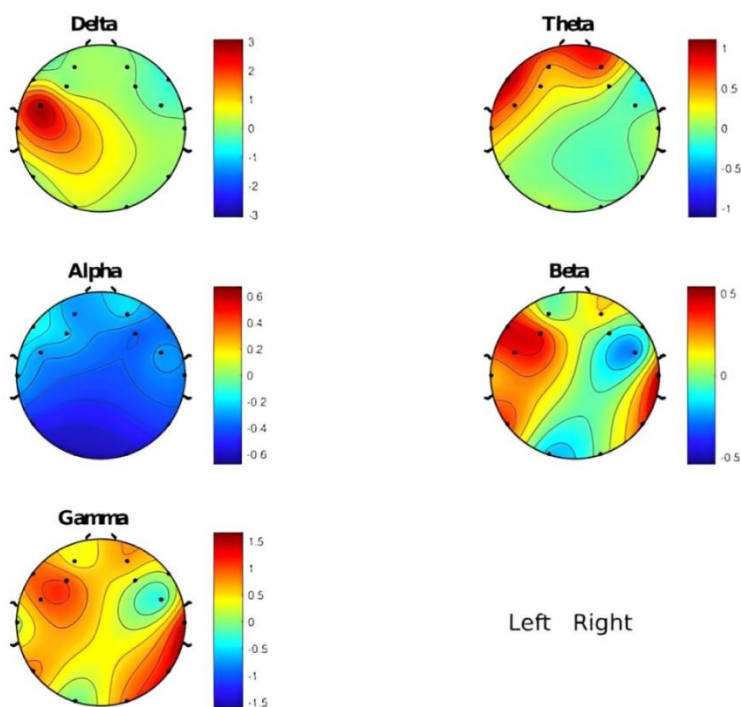


Figure 4.2: Topographic Maps of Band Power Distributions for Delta, Theta, Alpha, Beta, and Gamma Waves [105]

This technique measures the power within specific frequency bands to quantify the intensity of brain activity. By analyzing band power, researchers can assess the activity level in different cognitive states, such as relaxation or concentration. Fig. 4.2 [105] depicts the band power distributions for Delta, Theta, Alpha, Beta, and Gamma waves, visually representing their relative intensities [106].

### Connectivity Analysis

Connectivity analysis examines the interactions between different brain regions. Coherence and phase synchronization help determine how different brain areas communicate and coordinate during various cognitive tasks. This analysis is crucial for understanding functional brain networks and their role

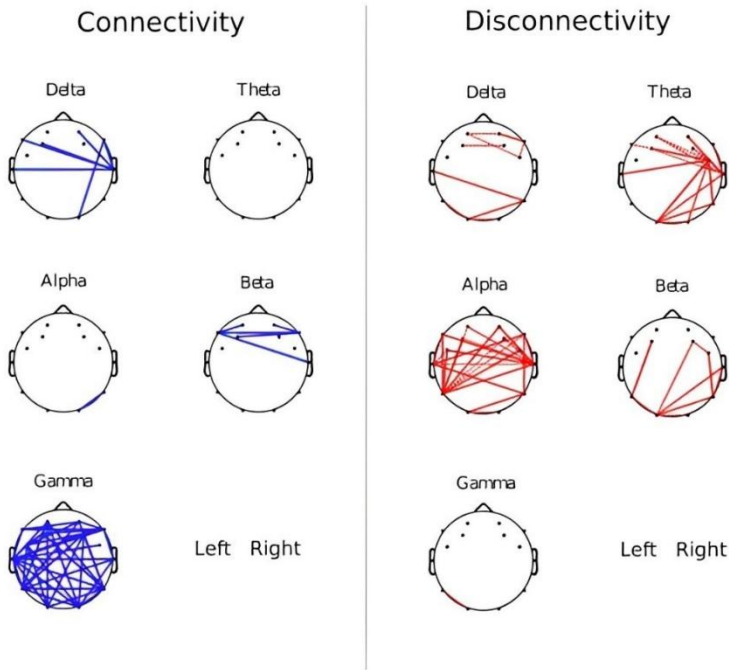


Figure 4.3: Connectivity and Dysconnectivity Patterns Across Different EEG Frequency Bands [95]

in cognitive processes. Fig. 4.3 [95] shows the connectivity and dysconnectivity patterns in the brain for different EEG frequency bands, highlighting the communication pathways and their alterations in various states [108].

Classifying EEG into different frequency bands allows us to link specific brain wave patterns with various cognitive states and functions. Analytical techniques such as band power and connectivity analysis provide deeper insights into brain activity, enhancing our understanding of neural processes and advancing the field of neuroengineering.

In addition to band power and connectivity analysis, time-frequency analysis (TFA) is a powerful technique used in EEG studies. TFA, including methods like wavelet transforms, allows researchers to see how the frequency content

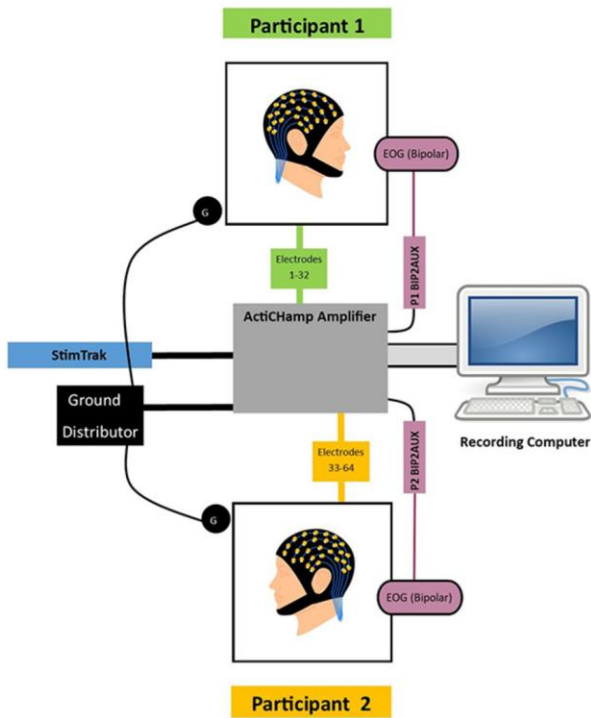


Figure 4.4: Schematic Diagram of an EEG Machine [110]

of a signal changes over time. This technique is especially useful for identifying transient events, such as short bursts of brain activity, which are crucial in understanding cognitive processes. TFA provides a detailed view of the brain's dynamic activity by decomposing EEG signals into constituent frequencies and observing their temporal evolution [109].

## Components of EEG System

An EEG system comprises several critical components that capture and analyze the brain's electrical activity. These components include electrodes, amplifiers, and data acquisition systems. Each element plays a unique role in ensuring accurate and reliable EEG recordings. The schematic diagram in Fig. 4.4 [110] illustrates the overall configuration of an EEG machine used for

recording data from multiple participants, providing a visual overview of its main components and their interactions.

## ***Electrodes: Types and Materials***

Electrodes are the primary interface between the EEG system and the scalp, capturing the electrical signals generated by neuronal activity. There are various types of electrodes, each suited for specific applications:

### **Surface Electrodes**

These are the most used in clinical and research settings. They are typically made from conductive materials such as silver/silver chloride (Ag/AgCl) or gold, ensuring efficient signal transmission.

### **Needle Electrodes**

Used less frequently, these electrodes penetrate the skin to reach closer to the source of electrical activity. They are made from stainless steel or platinum and are used in specific diagnostic procedures.

### **Dry Electrodes**

These electrodes do not require conductive gel, making them suitable for quick setups and repeated use. They are often made from materials like titanium or conductive polymers.

The electrode type and material choice depend on factors such as the required signal quality, the duration of recording, and patient comfort.

## ***Amplifiers: Function and Specifications***

Amplifiers are essential in EEG systems as they boost the weak electrical signals picked up by the electrodes, making them suitable for analysis. The basic functions and specifications of amplifiers include:

### **Signal Amplification**

Amplifiers increase the amplitude of the electrical signals from the brain, which are typically in the microvolt range.

### **Noise Reduction**

High-quality amplifiers are designed to minimize electrical noise and interference, ensuring a clear and accurate signal.

### Frequency Response

Amplifiers must have an appropriate frequency response to capture the wide range of brain wave frequencies, from delta to gamma waves.

### Channel Capacity

The number of channels an amplifier supports is crucial, as it determines how many electrodes can be simultaneously recorded.

## ***Data Acquisition Systems***

Modern data acquisition systems (DAS) for EEG integrate seamlessly with software platforms that enhance user experience. User-friendly interfaces allow researchers to set up and monitor experiments easily. Advanced software tools offer real-time data visualization, automated artifact detection, and sophisticated analysis capabilities. This integration ensures that data collection is efficient and the resulting data can be quickly and accurately analyzed, facilitating faster research and clinical practice advancements.

Critical features of DAS include:

### Analog-to-Digital Conversion (ADC)

This process involves converting continuous electrical signals into discrete digital values, enabling computerized analysis.

### Sampling Rate

The sampling rate must be sufficiently high to capture the nuances of brain activity. Typically, EEG systems use sampling rates ranging from 250 Hz to several kHz.

### Data Storage and Transfer

Modern DAS can store large amounts of data and transfer it to computers or cloud-based systems for real-time analysis and long-term storage.

## ***Setup and Configuration***

Proper setup and configuration of the EEG system are vital for obtaining accurate and reliable recordings. This involves careful electrode placement and scalp preparation.

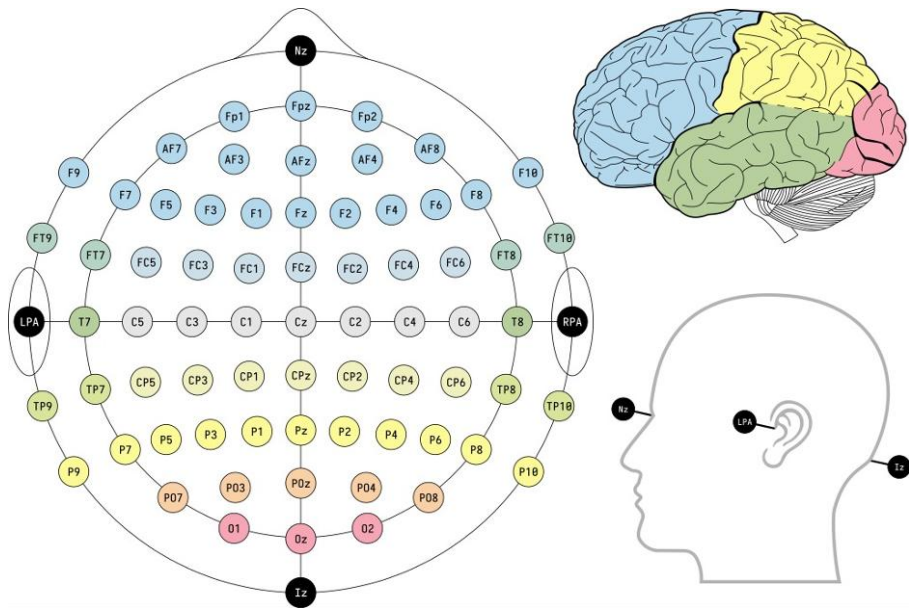


Figure 4.5: The 10-20 System for Electrode Placement in EEG [111]

## Electrode Placement

Electrode placement is guided by standardized systems such as the 10- 20 system, which ensures consistent and replicable results.

### Key points include

#### Anatomical Landmarks

Electrodes are placed on the scalp based on specific anatomical landmarks, ensuring standardized individual positioning.

#### Number of Electrodes

Depending on the study or clinical requirement, the number of electrodes can vary from a few (e.g., 8 or 16) to a full cap with 64 or more electrodes.

#### Placement Techniques

Techniques include using conductive gel or paste to enhance signal quality and secure the electrodes.

Accurate electrode placement is crucial for obtaining high-quality EEG data. Misplaced electrodes can lead to incorrect data interpretation and affect the reliability of the results. For example, improper placement may miss key brain regions associated with specific cognitive tasks, leading to incomplete or misleading conclusions.

### ***Scalp Preparation***

Scalp preparation is crucial for reducing impedance and improving signal quality. This process typically involves:

#### **Cleaning the Scalp**

The scalp is cleaned with an abrasive gel or solution to remove oils and dead skin cells, reducing the impedance between the scalp and electrodes.

#### **Applying Conductive Gel**

Conductive gel ensures a good connection between the electrodes and the scalp, facilitating efficient signal transmission.

### ***The 10-20 System***

The 10-20 system is a standardized method for placing electrodes on the scalp in EEG. This system ensures consistent and reproducible electrode placements across individuals and studies, facilitating reliable data collection and analysis [96]. The 10-20 system refers to electrode positioning based on the relative distances between specific anatomical landmarks on the scalp. The name "10-20" indicates that the distances between adjacent electrodes are 10% or 20% of the skull's total front-back or right-left distance. This method ensures that electrode placement is systematic and standardized. Electrodes are placed at intervals of 10% or 20% of the total length of the scalp, measured from the nasion (the bridge of the nose) to the inion (the bony bump at the back of the head) and from the left to the right preauricular points (just above the ears). Key positions include:

- Fp1, Fp2: Frontopolar positions
- Fz, Cz, Pz, Oz: Midline positions from front to back
- F3, F4, C3, C4, P3, P4, O1, O2: Lateral positions over the frontal, central, parietal, and occipital lobes

This systematic approach ensures that EEG recordings are consistent and comparable across sessions and subjects. The diagram in Fig. 4.5 [111] illustrates the 10-20 system, highlighting the placement of electrodes based on specific percentages of the head's total circumference and dimensions.

**Signal Resolution and Sampling Rates**

Signal resolution in EEG refers to the system's ability to detect and distinguish small changes in electrical activity on the scalp, which is crucial for identifying subtle brain processes. The higher signal resolution allows for a more precise and detailed representation of neural activity, which is essential for accurate analysis. Higher-resolution EEG recordings show more defined and distinct waveforms, capturing finer details of neural events. Conversely, lower-resolution recordings appear more blurred and less precise, potentially missing critical neural signals. This distinction underscores the importance of high-quality electrodes, amplifiers, and signal processing in achieving optimal

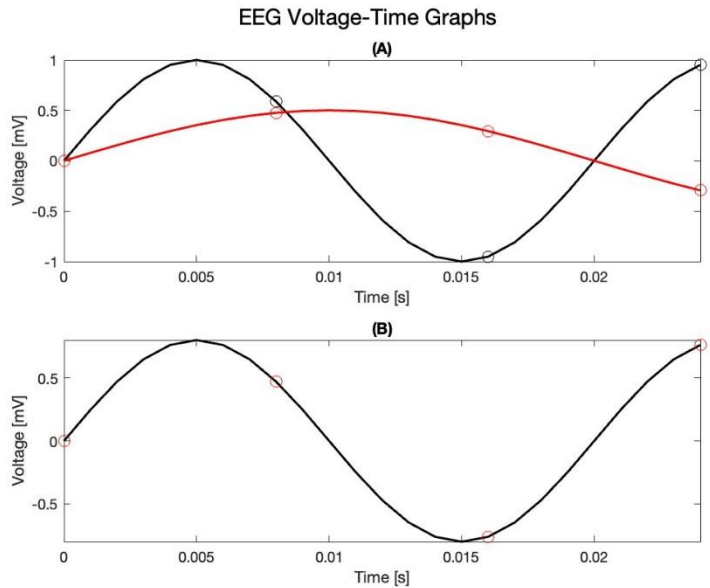


Figure 4.6: MATLAB plot of EEG sampling rates. Red circles represent the sampled data points, while the black line represents the actual signal

signal resolution in EEG systems. We will discuss this more later in this chapter when we talk about noise in signals.

Fig. 4.6 illustrates the concept of sampling rates in EEG. The sampling rate refers to the frequency at which the EEG system records data points per second. In the image, two different sampling rates are depicted:

1. Panel (A): This panel shows EEG data sampled at a lower rate. The red circles represent the recorded data points. Due to the lower sampling rate, the recorded data points are sparse and miss some details of the actual waveform (black line). This can result in aliasing, where the actual signal is not accurately represented.
2. Panel (B): This panel shows that the EEG data was sampled at a higher rate. The red circles, representing the recorded data points, are much closer together, capturing the waveform's finer details. This higher sampling rate provides a more accurate and detailed representation of the neural activity.

Higher sampling rates allow for a more detailed and accurate representation of neural activity, capturing rapid changes and transient events. Conversely, lower sampling rates may miss these details, leading to a less precise signal representation. This distinction is crucial in EEG to ensure the accurate detection and analysis of brain activity, especially for studies involving fast neural dynamics.

## ***MEG Operational Principles***

Magnetoencephalography (MEG) is a non-invasive neuroimaging technique used to measure the magnetic fields produced by neuronal activity in the brain. Unlike electroencephalography (EEG), which detects electrical activity, MEG captures the magnetic signals, providing high temporal and spatial resolution. This makes MEG an invaluable tool for studying brain function and diagnosing neurological disorders.

### ***Biomagnetic Signal Detection***

Biomagnetic signal detection in MEG involves capturing the minute magnetic fields generated by the electrical currents of active neurons. These magnetic fields are fragile, often in the femto-cell range, and require susceptible detectors

known as Superconducting Quantum Interference Devices (SQUIDs) to be accurately measured.

### ***Setup Considerations***

Setting up an MEG system involves several critical considerations to ensure optimal performance and accurate data acquisition. These include the room and environmental requirements, system calibration, and ensuring all components are correctly installed and maintained.

### ***Components of the MEG System***

Fig. 4.7 [112] illustrates the key components of an MEG system, specifically focusing on the SQUID (Superconducting Quantum Interference Device) and its associated circuitry. Each element is critical in accurately detecting and measuring the brain's magnetic fields [113].

#### **Pickup Coil**

The pickup coil is the initial component that detects the magnetic fields generated by neuronal activity. These coils are sensitive to the tiny magnetic signals produced by the brain.

#### **Input Coil**

The input coil is connected to the pickup coil and transfers the detected magnetic signal to the SQUID.

#### **SQUID**

The SQUID is at the core of the MEG system. It is susceptible and can detect minimal changes in magnetic fields. The SQUID operates at cryogenic temperatures, maintained by liquid helium (LHe), to ensure superconducting properties.

#### **Feedback Coil**

The feedback coil works with the SQUID to maintain a stable measurement environment by applying feedback current to cancel out the detected magnetic fields. This helps keep the SQUID's linearity and sensitivity.

## Heater

The heater occasionally warms the SQUID to reset its superconducting state if it becomes saturated.

## Pre-amplifier

The pre-amplifier boosts the signal from the SQUID before further processing. This is crucial as the signals detected are feeble and need amplification for accurate measurement.

## Integrator

The integrator processes the amplified signal, smoothing out the fluctuations and providing a continuous output signal.

## Voltage Offset

This component adjusts the signal's baseline voltage to ensure accurate readings and compensation for any drifts in the signal.

## Feedback Resistor

The feedback resistor helps control the feedback current applied to the feedback coil, which is essential for the measurement's stability and accuracy.

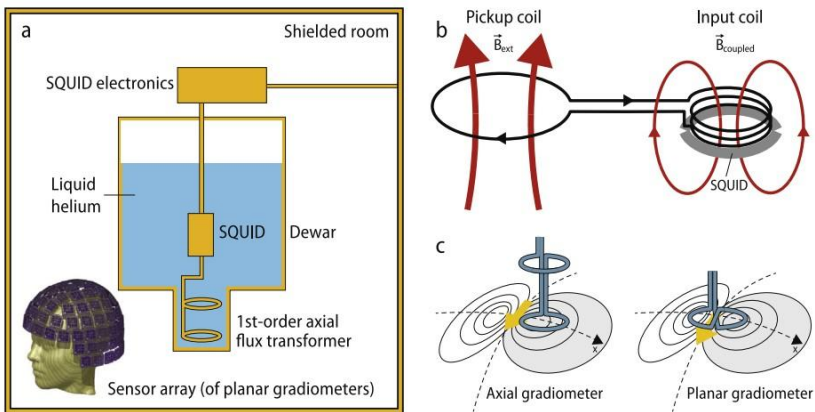


Figure 4.7: Block Diagram of Key Components in a MEG System a) A single channel axial gradiometer with SWID inside a dewar filled with liquid helium b) Flux Transformer and SQUID c) Axial and planar gradiometers [112]

### Bias Flux and Bias Current

These provide the necessary operating conditions for the SQUID, ensuring it functions within its optimal parameters.

### FLL (Flux Locked Loop) Switch

This switch helps maintain the SQUID in a flux-locked state, ensuring linearity and sensitivity in the measurements.

### Reset Switch

The reset switch resets the SQUID if it exceeds its operational range, ensuring continuous and accurate measurements.

### ***Room and Environmental Requirements***

The MEG system must be in a magnetically shielded room to prevent external magnetic interference. These rooms typically use multiple layers of metal and aluminum to protect against environmental noise. Additionally, the room should be acoustically insulated to minimize noise affecting sensitive measurements. Environmental controls, such as temperature and humidity regulation, are essential for optimal operating conditions.

### ***Event-Related Potentials (ERPs)***

Event-related potentials (ERPs) are the brain's electrical responses directly relating to specific sensory, cognitive, or motor events. These responses are time-locked, meaning they are consistently triggered at specific times after a particular event. ERPs are typically measured using electroencephalography (EEG), which records electrical activity from the scalp.

Two main features characterize ERPs:

- Latency: The timing of the ERP response, measured in milliseconds, indicates how quickly the brain responds to the event.
- Amplitude: The strength or size of the electrical response, which reflects the intensity of the brain's activity related to processing the event.

Fig. 4.8 [114] illustrates the various components of ERPs, highlighting the different waves and their associated cognitive functions:

- N1 Component: An early negative wave associated with initial sensory processing.
- P2 Component: A positive wave following N1, related to early perceptual processing.
- N2 Component: A negative wave involved in cognitive control and conflict monitoring.
- P3 Component: A positive wave linked to attention and decision-making processes.
- N400 Component: A negative wave associated with language and semantic processing.
- Late Positive Component (LPC): A late positive wave involved in memory and higher-order cognitive processes.

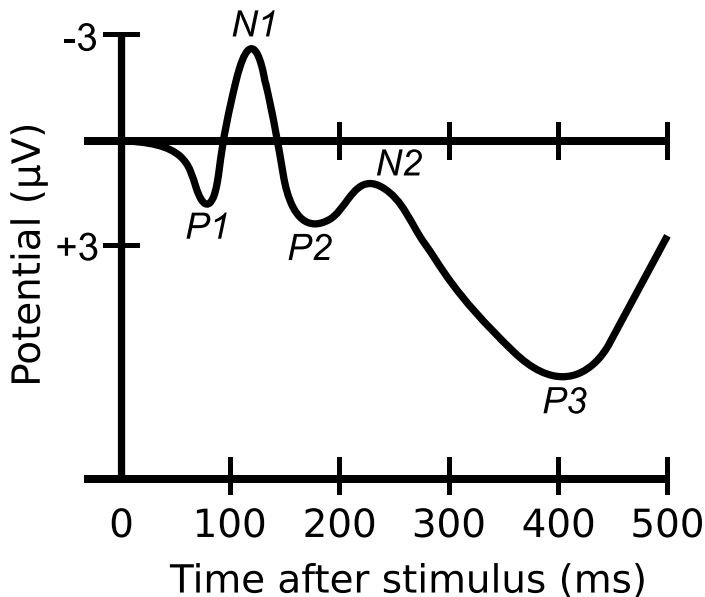


Figure 4.8: Components of ERP Sourced [114]

## Types of ERPs

### P300

Associated with attention and decision-making, typically elicited in oddball paradigms where subjects detect infrequent targets among frequent non-targets.

### N400

Linked to language processing and semantic incongruities, observed when a word or sentence is semantically unexpected.

ERN (Error-Related Negativity) is related to error detection and response monitoring and occurs when a person makes a mistake.

## Applications in Research and Clinical Practice

ERPs and MEG have significant applications in both research and clinical practice. The image illustrates the combined use of MEG and EEG in clinical settings, highlighting their complementary strengths in diagnosing and monitoring neurological conditions.

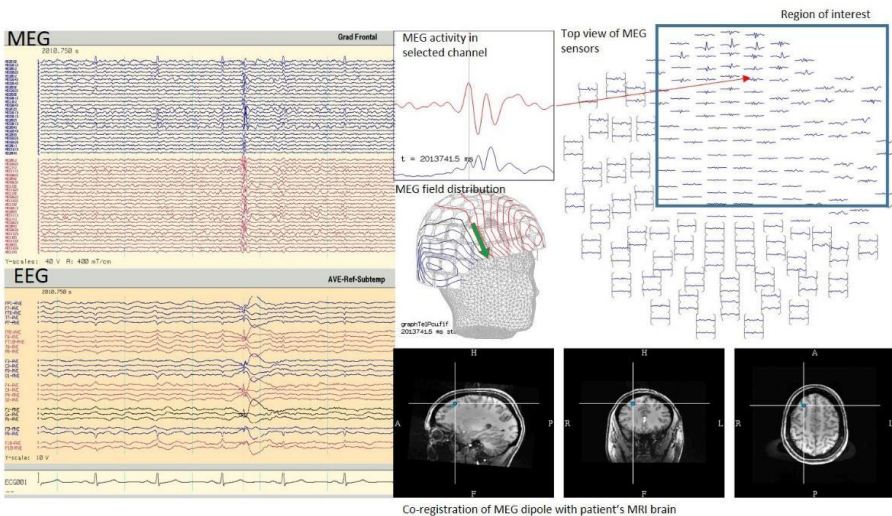


Figure 4.9 Combined EEG and MEG in Clinical Practice [115]

### ***Cognitive Function Analysis***

ERPs are extensively used in cognitive neuroscience to study brain processes such as perception, attention, memory, and language. Researchers can infer the neural mechanisms underlying various cognitive functions by analyzing ERP components' timing (latency) and amplitude. For example, the P300 component is used to study attention and working memory, while the N400 component is used to investigate language comprehension and semantic processing. With its high spatial resolution, MEG complements ERP studies by providing precise localization of neural activity, offering a comprehensive understanding of brain function. Fig. 4.9 [115] demonstrates the application of MEG and EEG in clinical practice, showing their utility in diagnosing and monitoring neurological conditions [116]. Each part of the image is explained below:

1. **MEG Recordings (Top Left):** This section shows the MEG signals recorded from various sensors around the head. These signals capture the magnetic fields generated by neuronal activity. The displayed waveforms represent brain activity over time, indicating areas of interest where abnormal activity may be present.
2. **EEG Recordings (Bottom Left):** This section displays EEG signals recorded from electrodes on the scalp. EEG captures the electrical activity of the brain, providing high temporal resolution. The waveforms here show brain activity and are used to identify abnormal patterns associated with neurological conditions.
3. **MEG Activity in Selected Channel (Top Center):** This part of the image zooms in on a specific channel's MEG activity, providing a detailed view of the magnetic field changes over time. This focused view helps analyze the characteristics of neural responses in a specific brain region.
4. **Top View of MEG Sensors (Top Right):** This diagram shows the layout of MEG sensors positioned around the head. Each sensor's location is mapped to ensure comprehensive brain coverage, allowing for precise localization of magnetic signals.

5. Region of Interest (Top Right Box): Highlighted within the top view of MEG sensors, this box indicates the specific area of the brain being closely examined. It shows the distribution of
6. MEG signals within this region help to pinpoint areas of abnormal activity.
7. MEG Field Distribution (Center Right): This section visualizes the magnetic field distribution detected by MEG sensors. The field lines and arrows represent the direction and intensity of the magnetic fields, providing insights into the underlying neural activity.
8. Co-registration of MEG Dipole with Patient's MRI Brain (Bottom Right): This set of images shows the co-registration of MEG data with the patient's MRI scans. Combining MEG's functional data with MRI's structural information allows for precise localization of neural sources within the anatomical context. This is particularly useful in pre-surgical planning for epilepsy patients, where accurate localization of epileptic foci is critical.



Figure 4.10: Illustration showing environmental interference affecting EEG and MEG recordings. Sources like power lines, electronic devices, and the Earth's magnetic field are depicted as waves or signals interfering with EEG and MEG data. Arrows indicate the interference direction towards the EEG and MEG devices, highlighting the impact of these external sources on the recordings. Image generated with AI.

By examining each part of the image, we can see how MEG and EEG recordings, along with their integration with MRI data, provide comprehensive insights into brain function and abnormalities. This multi-modal approach enhances the diagnosis and monitoring of neurological conditions, facilitating better clinical outcomes. Fig. 4.10 shows common environmental interferences affecting EEG and MEG recordings.

## Noise Considerations

### Sources of Noise in EEG and MEG

**Environmental Interference:** EEG and MEG systems are susceptible to environmental interference from external sources such as power lines, electronic devices, and the Earth's magnetic field. This noise can significantly distort the recorded signals, making it difficult to interpret the underlying neural activity accurately.

**Biological Artifacts:** Biological artifacts are significant noise sources in EEG and MEG recordings, originating from physiological activities such as eye movements, blinks, muscle activity, and cardiac signals. Fig. 4.11 [106] illustrates how these artifacts combine with the accurate EEG signal to form the observed EEG data. Eye movements and blinks produce low-frequency

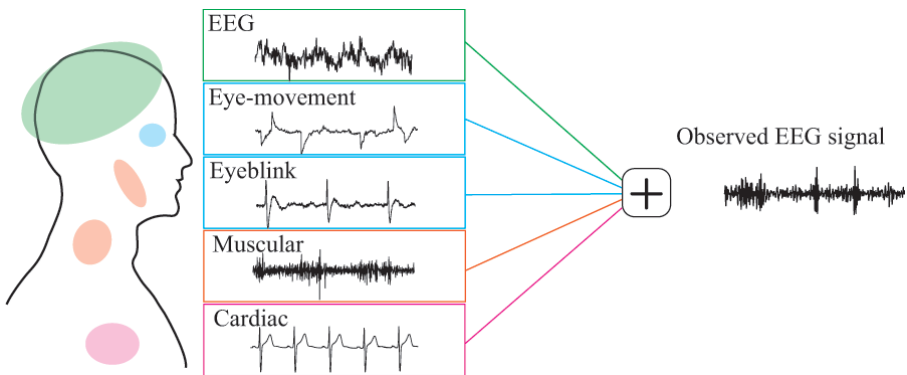


Figure 4.11: Illustration of Biological Artifacts Affecting EEG Signal - The image shows how various sources of biological artifacts, including eye movements, eye blinks, muscle activity, and cardiac signals, combine with the true EEG signal to form the observed EEG data. [106]

drifts and rapid spikes, respectively, while muscle activity generates high-frequency noise, and cardiac signals create rhythmic pulses. These artifacts can significantly distort the EEG signal, complicating the interpretation of neural activity. Understanding these noise sources is crucial for applying artifact rejection and filtering techniques to enhance the accuracy of EEG and MEG recordings.

***Strategies for Minimizing Noise***

**Shielding Techniques:** To combat environmental interference, MEG systems are typically housed in magnetically shielded rooms. These rooms are constructed with mu-metal and aluminum to block external magnetic fields. For EEG, proper grounding and shielded cables can help reduce electrical interference.

**Signal Processing Approaches:** Advanced signal processing techniques are employed to filter out noise and enhance the quality of the recorded data. This includes using digital filters to remove unwanted frequencies and algorithms

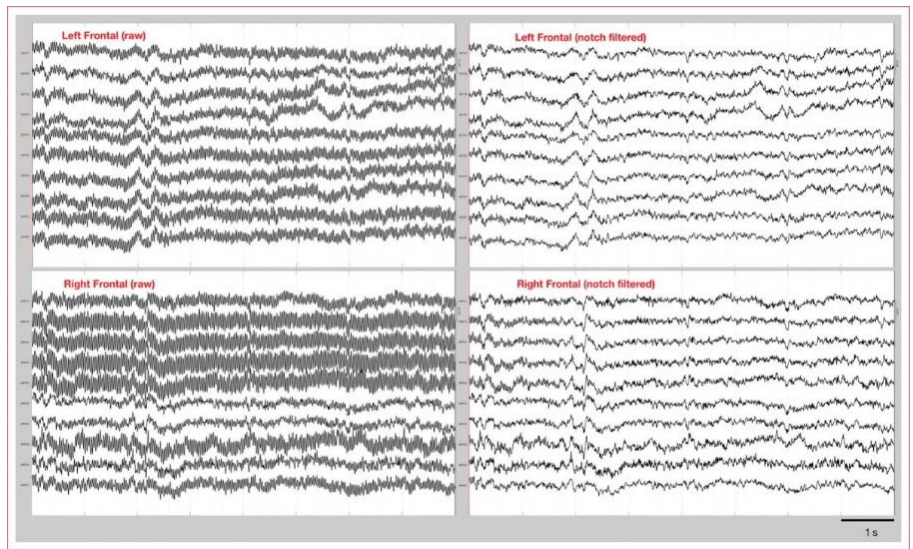


Figure 4.12: Comparison of Raw and Notch Filtered EEG Signals [118]

to identify and reject artifacts. Techniques such as Independent Component Analysis (ICA) can be particularly effective in separating neural signals from noise.

## ***MEG/EEG Software***

### ***Signal Processing Tools***

#### **Filtering**

Filtering is a fundamental signal processing tool that removes noise from EEG and MEG data. High-pass filters can eliminate low-frequency noise, while low-pass filters remove high-frequency noise [117]. Band-pass filters are used to isolate specific frequency bands of interest.

#### **Artifact Rejection**

Artifact rejection algorithms identify and remove non-neural signals from the data. Techniques such as Independent Component Analysis (ICA) and Principal Component Analysis (PCA) can separate artifacts from neural signals, improving the clarity and accuracy of the recordings.

Fig. 4.12 [118] shows EEG recordings from the left and right frontal areas, comparing raw data (left panels) with notch-filtered data (right panels). Notch filters remove specific frequencies, such as power line noise (e.g., 50/60 Hz), which can significantly distort the EEG signal. The raw data panels display high noise levels, making it difficult to discern the underlying neural activity. In contrast, the notch-filtered panels show a cleaner signal with reduced noise, allowing for a more straightforward interpretation of neural activity. This demonstrates the effectiveness of filtering in enhancing the quality of EEG recordings by eliminating unwanted noise [118].

### ***Analysis Software***

#### **Time-Frequency Analysis**

Time-frequency analysis methods, such as wavelet transforms and short-time Fourier transforms, allow researchers to examine how the frequency content of neural signals changes over time. This is crucial for studying dynamic neural processes and understanding how different brain rhythms are involved in various cognitive functions.

#### **Source Localization Techniques**

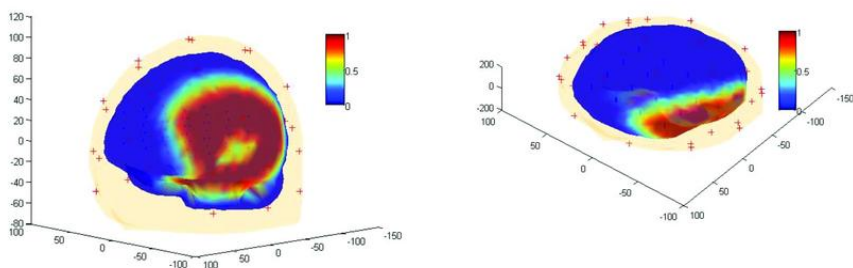


Figure 4.13: Brain Mapping for Real EEG Signals [119]

Source localization techniques aim to pinpoint the origins of neural activity within the brain. Methods like beamforming and equivalent current dipole modeling use the recorded data to estimate the spatial location of neural sources, enhancing the spatial resolution of EEG and MEG.

### ***Visualization Tools***

#### **Brain Mapping**

Brain mapping tools visually represent neural activity across different brain regions. These maps help researchers and clinicians understand the spatial distribution of brain functions and identify areas affected by neurological conditions. The image shows brain mapping for accurate EEG signals, highlighting areas of varying neural activity. The color scale indicates the intensity of the signals, with different colors representing different activity levels. This visual representation allows for easy identification of active brain regions and can be crucial for diagnosing and monitoring neurological disorders. Fig. 4.13 [119] illustrates the spatial distribution of neural activity across the brain, as captured by EEG recordings. The color scale, ranging from blue (low activity) to red (high activity), clearly visualizes which brain areas are most active. Brain mapping tools like this are essential for understanding different brain regions' complex functions and identifying abnormalities in clinical settings [120].

#### **Real-Time Data Display**

Real-time data display tools provide immediate feedback on ongoing brain activity, allowing researchers to monitor experiments and adjust on the fly.

This capability is handy in clinical settings for real-time diagnostics and monitoring, enabling quick responses to changes in a patient's neural activity and facilitating immediate intervention when necessary.

### ***Advantages and Disadvantages***

#### **EEG**

Pros: EEG is noninvasive, cost-effective, and offers high temporal resolution, making it suitable for studying rapid neural processes. Due to its accessibility and ease of use, it is widely used in research and clinical settings.

Cons: EEG has lower spatial resolution than MEG, as the skull and scalp distort electrical signals. It is also susceptible to various artifacts from muscle activity and environmental noise, which can complicate data interpretation [121].

#### **MEG**

Pros: MEG provides high spatial and temporal resolution, allowing for precise localization of neural activity. It is non-invasive and can detect minute magnetic fields generated by neuronal currents without affecting the skull or scalp.

Cons: MEG systems are expensive and require specialized facilities, including magnetically shielded rooms and cryogenic cooling systems. The operational and infrastructure requirements can limit their accessibility compared to EEG [122].

## **Chapter 4: Summary**

In this chapter, we have delved into the fundamental roles of Electroencephalography (EEG) and Magnetoencephalography (MEG) in neuroengineering. These noninvasive techniques are crucial for recording and analyzing the brain's electrical and magnetic activities. They provide critical brain function insights and advance research and clinical practice.

We started by exploring the importance of different EEG frequency bands and their associations with various cognitive states. Understanding the setup and configuration of EEG systems, including electrode placement and scalp preparation, is essential for acquiring high-quality data. We also examined

EEG systems' components and technical specifications, such as electrodes, amplifiers, and data acquisition systems, emphasizing their roles in ensuring accurate neural recordings. In detail, we discussed the operational principles of MEG, including biomagnetic signal detection and system setup considerations. We highlighted the essential components of MEG systems, such as SQUID sensors and cooling systems, and the room and environmental requirements necessary for optimal performance. Event-related potentials (ERPs) were explained, focusing on their definitions, components, and applications in cognitive function analysis and clinical diagnosis. Integrating MEG and EEG in clinical practice enhances the diagnosis and monitoring of neurological conditions, providing comprehensive insights into brain function and abnormalities. We also covered noise considerations, including environmental interference and biological artifacts, along with strategies for minimizing noise through shielding techniques and advanced signal processing approaches. The significance of MEG/EEG software tools, including filtering, artifact rejection, time-frequency analysis, and source localization techniques, was emphasized in improving the clarity and accuracy of neural recordings. Visualization tools like brain mapping and real-time data display further aid in understanding neural activity and facilitating clinical diagnostics. Finally, we evaluated the advantages and disadvantages of EEG and MEG. EEG is non-invasive, cost-effective, and offers high temporal resolution but is limited by low spatial resolution and susceptibility to artifacts. MEG provides high spatial and temporal resolution but requires expensive and specialized facilities.

As you conclude this chapter, I encourage you, as a neuroengineering professional, to seize the opportunity to impact EEG and MEG significantly. Your innovative research, technological advancements, and clinical applications can drive forward our understanding of brain function, improve diagnostic and therapeutic outcomes, and contribute to the development of new tools and methodologies. Embrace the challenges and possibilities within this field and strive to push the boundaries of what we know about the brain, ultimately making a profound difference in science and healthcare. The future

of neuroengineering is bright, and your contributions can shape its course and legacy.



## Chapter 4: Learning activities

### Learning Activity 4.1

A concept map is a visual representation tool to organize and structure knowledge. It displays relationships between concepts in a graphical format, typically through nodes and connecting lines. Each node represents a concept, and lines (often labeled) illustrate the connections or relationships between these concepts.



#### Key Features of a Concept Map:

1. Nodes are usually circles or boxes containing key concepts or ideas.
2. Links: Lines or arrows that connect the nodes, showing how the concepts are related.
3. Labels: Words or phrases on the links describing the relationship between the connected concepts.
4. Hierarchy: Concept maps often have a hierarchical structure, with more general or broader concepts at the top and more specific or detailed concepts branching out below.
5. Cross-Links: These show relationships between concepts in different parts of the map, illustrating the complexity and interconnectivity of the ideas.

#### Benefits of Concept Maps:

1. Visual Learning: They help visualize the relationships between concepts, making complex information easier to understand.
2. Organization: They organize information in a clear, structured way, aiding memory and recall.
3. Critical Thinking: Creating concept maps requires critical thinking to determine the relationships and hierarchy among concepts.
4. Collaboration: They can be used collaboratively, with multiple people contributing to and discussing the map.
5. Problem-Solving: They help identify gaps in knowledge and can be used to plan and solve problems systematically.

## *Activity*

Individual activity: draw a concept map connecting the different 'brain' noninvasive continuous signals.

---

## **Learning Activity 4.2**

Project-Based Learning (PBL) is an educational approach that emphasizes hands-on, student-centered learning through extended projects that tackle real-world problems and challenges. This method engages students in active exploration and inquiry, allowing them to apply knowledge and skills practically and meaningfully. Projects are designed to be relevant to students' lives and interests, promoting deeper understanding and sustained engagement. Students often work in teams, fostering collaboration and communication skills, and they can take ownership of their learning by making choices about their project's direction and outcome. PBL is typically multidisciplinary, integrating various subjects and helping students see the connections between different areas of knowledge. The learning process culminates in a public product or presentation, allowing students to share their work with a broader audience. Reflective practice is also a key component, with students and teachers regularly assessing the learning outcomes and the learning process. PBL enhances critical thinking, problem-solving, and teamwork, making learning engaging and impactful.

Activity: propose the following: as a student engineer, you need to design a machine capable of generating EEG data; how would you do it?

Step 1: form teams of 3 students

Step 2: discuss with the rest of the class how many different approaches were found.

---



## Learning Activity 4.3

Similar to the previous activity: "PBL: a pilot is getting drowsy, you are asked as an engineer to address the issue; how can you use what you have learned so far to create a device that solves the problem? Show an FBD"



Step 1: form teams of 3 students

Step 2: discuss with the rest of the class how many different approaches were found.



## Chapter 4: Lab introduction

In this series of lab exercises, you will gain hands-on experience with EEG signal processing and analysis using MATLAB. These labs are designed to apply your understanding of electroencephalography (EEG) data processing through practical applications.

In the first lab, you will follow a step-by-step laboratory exercise using MATLAB to perform EEG signal processing. Utilizing the Signal Processing Toolbox, you will generate and analyze EEG signals, simulate different brain states, add noise, amplify signals, apply filters, and visualize the results. By the end of this lab, you will be proficient in handling EEG data and using various signal-processing techniques to interpret brain activity.

The second lab introduces you to EEGLAB, a MATLAB toolbox specifically designed for processing EEG and MEG. Distributed under the free BSD license, EEGLAB provides a comprehensive suite of tools for displaying and analyzing EEG data. You will become familiar with the toolbox's capabilities, learning to process and visualize complex electrophysiological data effectively. This lab will equip you with essential advanced EEG data analysis skills, preparing you for further research and applications in neuroscience and biomedical engineering.



# Chapter 4: Lab Example 1



Following this step-by-step laboratory exercise, MATLAB will be used to perform the EEG signal processing, as illustrated in your example. You will need the Signal Processing Toolbox to complete this lab. By the end of the exercise, you should be able to generate and analyze EEG signals, simulate different brain states, add noise, amplify signals, apply filters, and visualize the results.

## ***EEG Signal Processing in MATLAB***

### ***Objective***

This exercise aims to understand and analyze EEG signals by generating synthetic EEG signals, simulating different brain states, adding noise, amplifying signals, filtering, and visualizing the results.

### ***Materials Needed***

- MATLAB software
- Signal Processing Toolbox
- Computer with sufficient computational capabilities

### ***Exercise Instructions***

#### Step 1: Set Up the MATLAB Environment

1. Open MATLAB.
2. Create a new script and name it 'EEG\_Signal\_Processing.m'.

#### Step 2: Define the Parameters

```
Fs = 1000; % Sampling frequency in Hz  
T = 10; % Duration of the signal in seconds  
t = 0:1/Fs:T-1/Fs; % Time vector
```

#### Step 3: Generate Awake and Drowsy EEG Signals

```
% Generate awake EEG signal with alpha and beta  
waves
```

```

awake_alpha_wave = 0.7 * sin(2*pi*10*t);
awake_beta_wave = 0.5 * sin(2*pi*20*t);
awake_eeg_signal = awake_alpha_wave +
awake_beta_wave;

% Generate normal drowsy EEG signal with lower
amplitude alpha and beta waves
drowsy_alpha_wave = 0.3 * sin(2*pi*10*t);
drowsy_beta_wave = 0.2 * sin(2*pi*20*t);
drowsy_eeg_signal = drowsy_alpha_wave +
drowsy_beta_wave;

```

#### Step 4: Simulate Epileptiform Activity in Drowsy EEG

```

epileptiform_start = 3; % Time point (in seconds)
to start epileptiform activity
epileptiform_duration = 1; % Duration of
epileptiform activity
epileptiform_amplitude = 1.5; % Amplitude of
epileptiform spikes

epileptiform_signal = zeros(size(t));
epileptiform_indices = find(t >= epileptiform_start
& t < (epileptiform_start +
epileptiform_duration));
epileptiform_signal(epileptiform_indices) =
epileptiform_amplitude *
square(2*pi*5*(t(epileptiform_indices)-
epileptiform_start));

drowsy_eeg_with_epileptiform = drowsy_eeg_signal +
epileptiform_signal;

```

#### Step 5: Add Noise to Simulate Real-World EEG Signals

```

noise_level = 0.1;
noisy_awake_alpha = awake_alpha_wave + noise_level
* randn(size(t));

```

```

noisy_awake_beta = awake_beta_wave + noise_level *
randn(size(t));
noisy_drowsy_alpha = drowsy_alpha_wave +
noise_level * randn(size(t));
noisy_drowsy_beta = drowsy_beta_wave + noise_level
* randn(size(t));
noisy_drowsy_with_epileptiform =
drowsy_eeg_with_epileptiform + noise_level *
randn(size(t));

% Combine noisy signals
awakeEEGSignal = noisy_awake_alpha +
noisy_awake_beta;
drowsyEEGSignal = noisy_drowsy_alpha +
noisy_drowsy_beta;
drowsyEEGWithEpileptiformSignal =
noisy_drowsy_with_epileptiform;

```

### Step 6: Amplify the Signals

```

amplificationFactor = 2;
amplifiedAwakeSignal = awakeEEGSignal *
amplificationFactor;
amplifiedDrowsySignal = drowsyEEGSignal *
amplificationFactor;
amplifiedDrowsyWithEpileptiformSignal =
drowsyEEGWithEpileptiformSignal *
amplificationFactor;

```

### Step 7: Design and Apply a Low-Pass FIR Filter

```

Fc = 30;           % Cutoff frequency
order = 100;       % Filter order

% Design a low-pass FIR filter
d = designfilt('lowpassfir', 'FilterOrder', order,
...

```

```

                                'CutoffFrequency', Fc, 'SampleRate',
Fs, ...
                                'DesignMethod', 'window', 'Window',
'hamming');

% Filter the amplified signals
filteredAmplifiedAwakeEEG = filter(d, amplifiedAwakeSignal);
filteredAmplifiedDrowsyEEG = filter(d, amplifiedDrowsySignal);
filteredAmplifiedDrowsyWithEpileptiformEEG = filter(d, amplifiedDrowsyWithEpileptiformSignal);

```

### Step 8: Apply Zero-Phase Filtering

```

filteredAmplifiedAwakeEEG_zeroPhase = filtfilt(d, amplifiedAwakeSignal);
filteredAmplifiedDrowsyEEG_zeroPhase = filtfilt(d, amplifiedDrowsySignal);
filteredAmplifiedDrowsyWithEpileptiformEEG_zeroPhase = filtfilt(d, amplifiedDrowsyWithEpileptiformSignal);

```

### Step 9: Plotting the Results

```

Fc = 30;           % Cutoff frequency
order = 100;       % Filter order

% Design a low-pass FIR filter
d = designfilt('lowpassfir', 'FilterOrder', order,
...
              'CutoffFrequency', Fc, 'SampleRate',
Fs, ...
              'DesignMethod', 'window', 'Window',
'hamming');

% Filter the amplified signals

```

```

filteredAmplifiedAwakeEEG = filter(d,
amplifiedAwakeSignal);
filteredAmplifiedDrowsyEEG = filter(d,
amplifiedDrowsySignal);
filteredAmplifiedDrowsyWithEpileptiformEEG =
filter(d, amplifiedDrowsyWithEpileptiformSignal);
```

```

### Step 10: Apply Zero-Phase Filtering

```

filteredAmplifiedAwakeEEG_zeroPhase = filtfilt(d,
amplifiedAwakeSignal);
filteredAmplifiedDrowsyEEG_zeroPhase = filtfilt(d,
amplifiedDrowsySignal);
filteredAmplifiedDrowsyWithEpileptiformEEG_zeroPhase = filtfilt(d,
amplifiedDrowsyWithEpileptiformSignal);

```

### Step 11: Plotting the Results

```

% Define a common y-axis range for all plots
yAxisRange = [-3.5, 3.5]; % This range might need
adjustment based on actual signal amplitudes

figure;
% Awake EEG Signals
subplot(4,3,1);
plot(t, awakeEEGSignal);
title('Awake EEG Signal');
xlabel('Time (s)');
ylabel('Amplitude');
ylim(yAxisRange);

subplot(4,3,4);
plot(t, amplifiedAwakeSignal);
title('Amplified Awake Signal');
xlabel('Time (s)');

```

```

ylabel('Amplitude');
ylim(yAxisRange);

subplot(4,3,7);
plot(t, filteredAmplifiedAwakeEEG);
title('Filtered Amplified Awake Signal');
xlabel('Time (s)');
ylabel('Amplitude');
ylim(yAxisRange);

subplot(4,3,10);
plot(t, filteredAmplifiedAwakeEEG_zeroPhase);
title('Zero-Phase Filtered Awake Signal');
xlabel('Time (s)');
ylabel('Amplitude');
ylim(yAxisRange);

% Normal Drowsy EEG Signals
subplot(4,3,2);
plot(t, drowsyEEGSignal);
title('Normal Drowsy EEG Signal');
xlabel('Time (s)');
ylabel('Amplitude');
ylim(yAxisRange);

subplot(4,3,5);
plot(t, amplifiedDrowsySignal);
title('Amplified Drowsy Signal');
xlabel('Time (s)');
ylabel('Amplitude');
ylim(yAxisRange);

subplot(4,3,8);
plot(t, filteredAmplifiedDrowsyEEG);
title('Filtered Amplified Drowsy Signal');
xlabel('Time (s)');
ylabel('Amplitude');
ylim(yAxisRange);

subplot(4,3,11);

```

```

plot(t, filteredAmplifiedDrowsyEEG_zeroPhase);
title('Zero-Phase Filtered Drowsy Signal');
xlabel('Time (s)');
ylabel('Amplitude');
ylim(yAxisRange);

% Drowsy EEG with Epileptiform Activity Signals
subplot(4,3,3);
plot(t, drowsyEEGWithEpileptiformSignal);
title('Drowsy EEG with Epileptiform Activity');
xlabel('Time (s)');
ylabel('Amplitude');
ylim(yAxisRange);

subplot(4,3,6);
plot(t, amplifiedDrowsyWithEpileptiformSignal);
title('Amplified Drowsy with Epileptiform Signal');
xlabel('Time (s)');
ylabel('Amplitude');
ylim(yAxisRange);

subplot(4,3,9);
plot(t,
filteredAmplifiedDrowsyWithEpileptiformEEG);
title('Filtered Amplified Drowsy with Epileptiform
Signal');
xlabel('Time (s)');
ylabel('Amplitude');
ylim(yAxisRange);

subplot(4,3,12);
plot(t,
filteredAmplifiedDrowsyWithEpileptiformEEG_zeroPhase);
title('Zero-Phase Filtered Drowsy with Epileptiform
Signal');
xlabel('Time (s)');
ylabel('Amplitude');
ylim(yAxisRange);

```

```
sgtitle('EEG Signals Processing: Awake vs. Normal  
Drowsy vs. Drowsy with Epileptiform Activity');
```

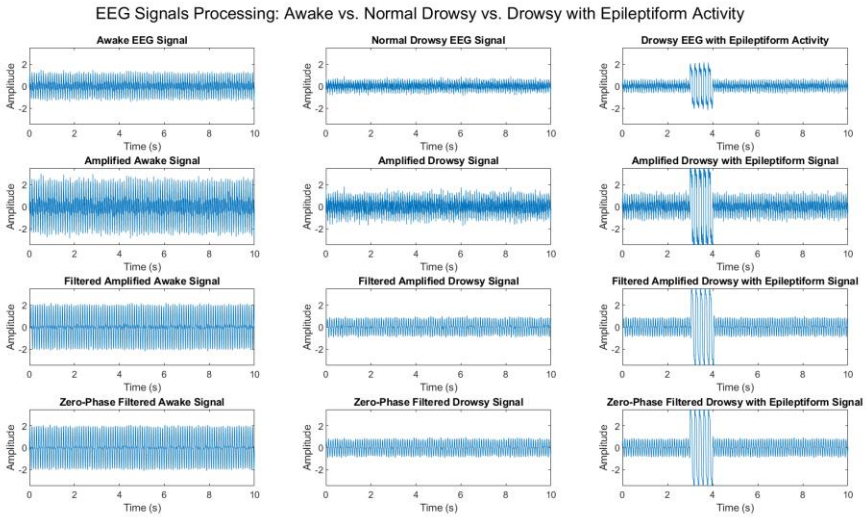


Figure 4.14: EEG Signal Results

## Results

### *Top Row: Original EEG Signals*

Awake EEG Signal: Shows the combination of alpha and beta waves.

Normal Drowsy EEG Signal: Lower amplitude alpha and beta waves indicate a drowsy state.

Drowsy EEG with Epileptiform Activity: A clear spike at the 3-second mark indicates epileptiform activity.

### *Second Row: Amplified EEG Signals*

Amplified Awake Signal: The awake signal is amplified, making the wave patterns more distinct.

Amplified Drowsy Signal: The drowsy signal is similarly amplified.

Amplified Drowsy with Epileptiform Signal: Amplified version of the drowsy signal with more pronounced epileptiform spikes.

### ***Third Row: Filtered Amplified EEG Signals***

Filtered Amplified Awake Signal: High-frequency noise is reduced, but the main characteristics of the awake signal are preserved.

Filtered Amplified Drowsy Signal: Similar noise reduction is observed.

Filtered Amplified Drowsy with Epileptiform Signal: Noise reduction while maintaining the epileptiform activity.

### ***Fourth Row: Zero-Phase Filtered Signals***

Zero-Phase Filtered Awake Signal: Provides a cleaner signal with preserved phase characteristics.

Zero-Phase Filtered Drowsy Signal: Shows a clear, filtered version of the drowsy state.

Zero-Phase Filtered Drowsy with Epileptiform Signal: Cleaned signal showing the epileptiform spikes clearly.

## ***Conclusion***

The provided MATLAB code and image demonstrate the steps in generating, amplifying, filtering, and visualizing EEG signals. Each stage highlights different aspects of signal processing, showing how noise can be mitigated and important signal characteristics preserved. This exercise is crucial for understanding how EEG data is processed and analyzed in practical applications.



## Chapter 4: Lab Example 2

In this lab, we will familiarize ourselves with EEGLAB, a MATLAB toolbox designed to process electroencephalography (EEG), magnetoencephalography (MEG), and other electrophysiological data. Distributed under the free BSD license, EEGLAB offers a comprehensive suite of tools for displaying and analyzing EEG data.



### *Installation and Main Features*

EEGLAB is hosted by the Swartz Center for Computational Neuroscience at UC San Diego. You can download the toolbox from this [link](#). We extend our gratitude to UC San Diego for providing this valuable resource.

### *Download and Installation*

The download and installation process is similar to that of other MATLAB toolboxes:

1. Visit the EEGLAB download page.
2. Follow the instructions provided to download the appropriate version for your system.
3. Unzip the downloaded file to a convenient directory on your computer.
4. Add the EEGLAB folder to your MATLAB path.

### *Running EEGLAB*

After installation, you can launch EEGLAB by running the `eeglab.m` file. To do this:

1. Open MATLAB.
2. Navigate to the directory where you unzipped EEGLAB.
3. Type `eeglab` in the MATLAB command window and press Enter. This action should open the EEGLAB graphical user interface (GUI), which will appear in Fig. 3.15.

In the following sections of this lab, we will explore the main features of EEGLAB for displaying and processing EEG data. These features

| Name                       | Date modified     | Type        | Size   |
|----------------------------|-------------------|-------------|--------|
| test_data                  | 7/24/2024 4:07 AM | File folder |        |
| eeglab_data.set            | 7/24/2024 4:07 AM | SET File    | 345 KB |
| eeglab_data_epochs_ica.set | 7/24/2024 4:07 AM | SET File    | 225 KB |

Figure 3.15: EEGLAB GUI

include data importing, preprocessing, visualization, and analysis tools essential for neuroengineering research.

If you select File- load the existing dataset and browse to the sample data folder in the toolbox, you will see that EEGLAB is a powerful tool for processing and analyzing EEG data and associated events. While you can import your own EEG data, we will work with existing datasets included in the EEGLAB package for this lab. To load a sample dataset, follow these steps:

1. Go to the File menu.
2. Select Load existing dataset.

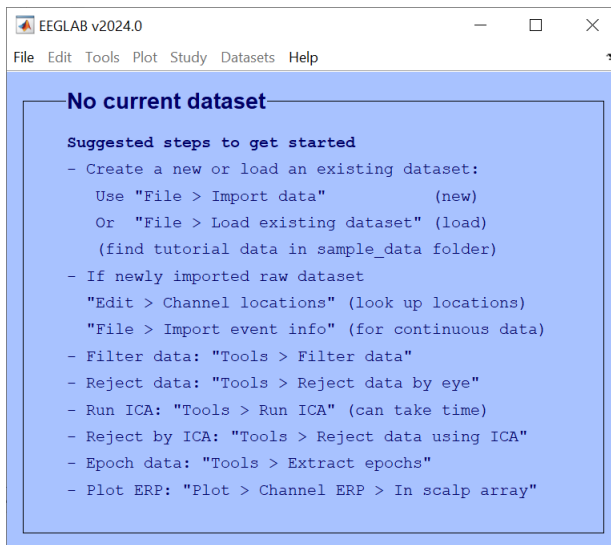


Figure 4.15: EEGLAB Data Set

3. Browse to the `sample_data` folder within the EEGLAB toolbox directory.
4. You will see several sample dataset options from which to choose. These sample datasets will help you familiarize yourself with the features and capabilities of EEGLAB (Fig. 4.15).

In this lab, we will work with the `eeglab_data.set` sample dataset.

As shown, the sample data contains over 30,000 frames per epoch, 32 channels per frame, and 154 events, and it is sampled at 128 Hz, meaning 128 samples per second (Fig. 4.16).

### *Loading the EEG Data*

1. Select **eeglab\_data.set** from the available options.
2. This dataset contains EEG data with 32 channels, each labeled accordingly. ##Visualizing the Data Once the data is loaded, EEGLAB

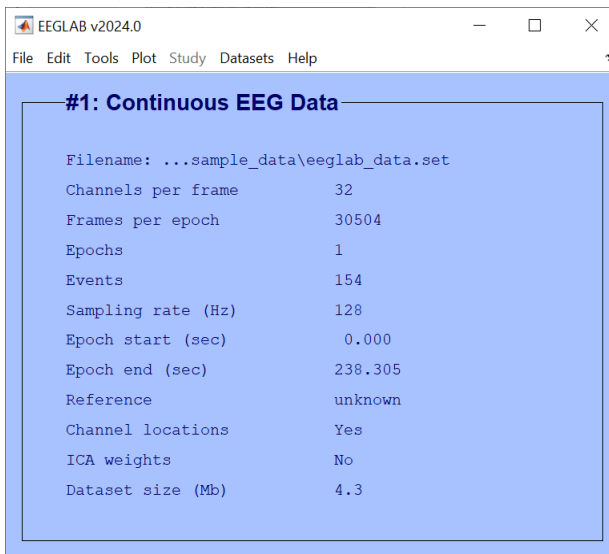


Figure 4.16: Sample Data for lab

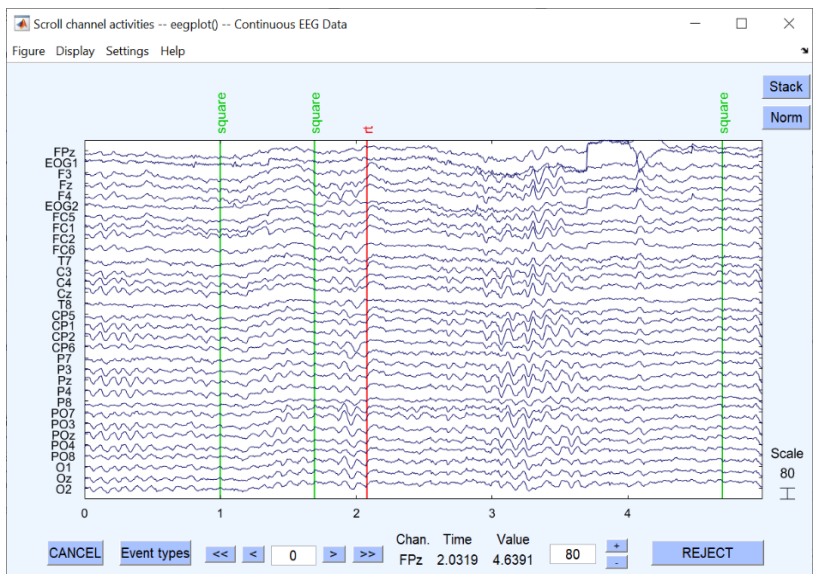


Figure 4.17: Channel Plots

allows you to plot all the channels in the time domain to observe different events (Fig. 4.17). In this dataset: Square events are highlighted in green. RT events are highlighted in red.

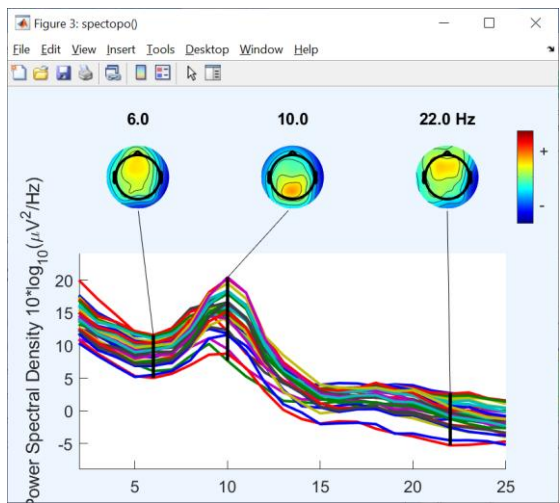


Figure 4.18: PSD Plot

# Power Spectral Density

EEGLAB also provides tools to plot the power spectral density (PSD) of the EEG signals (Fig. 4.18). This feature is useful for identifying channels that may be faulty or need to be excluded from the analysis.

# Inspecting Specific Channels

You can isolate a specific channel and visualize its properties using the **pop\_prop** function. This feature enables detailed inspection of individual channels, facilitating quick and efficient EEG data analysis (Fig. 4.19).

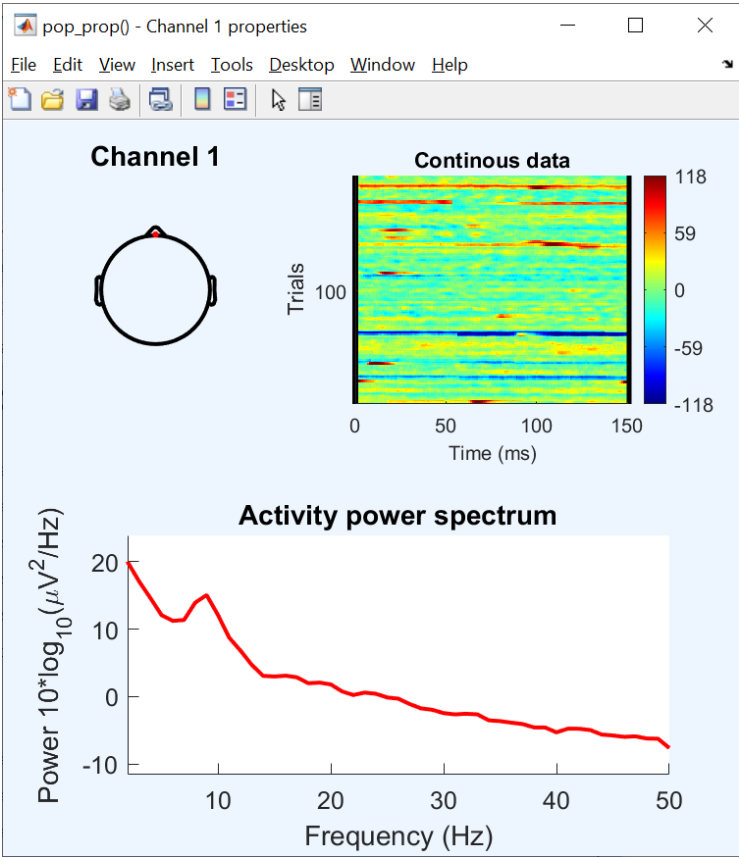


Figure 4.19: Isolating a channel

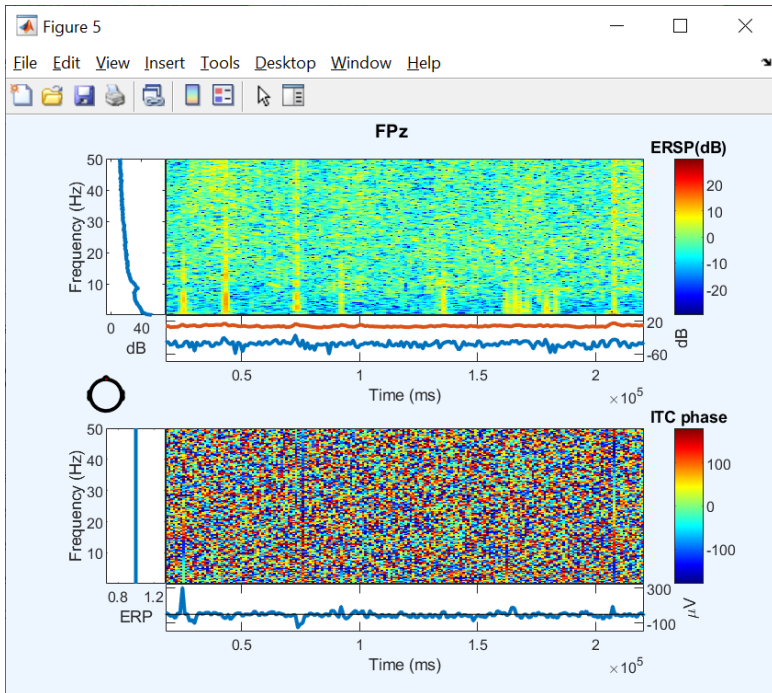


Figure 4.10: Advanced Features: Event Related Potentials

## Advanced Features

EEGLAB is a robust tool with a variety of advanced features:

- **Filtering:** EEGLAB allows you to apply frequency-delimited filters to the signals, which helps isolate specific frequency bands of interest.
- **Artifact Removal:** You can use independent component analysis (ICA) to remove artifacts from the data.
- **Event-Related Potentials (ERP):** EEGLAB enables the extraction and classification of event-related potentials (ERP), which are brain responses directly resulting from specific sensory, cognitive, or motor events (Fig. 4.20). By averaging the responses of all events, you can build a signature waveform that is distinctive of the response to a

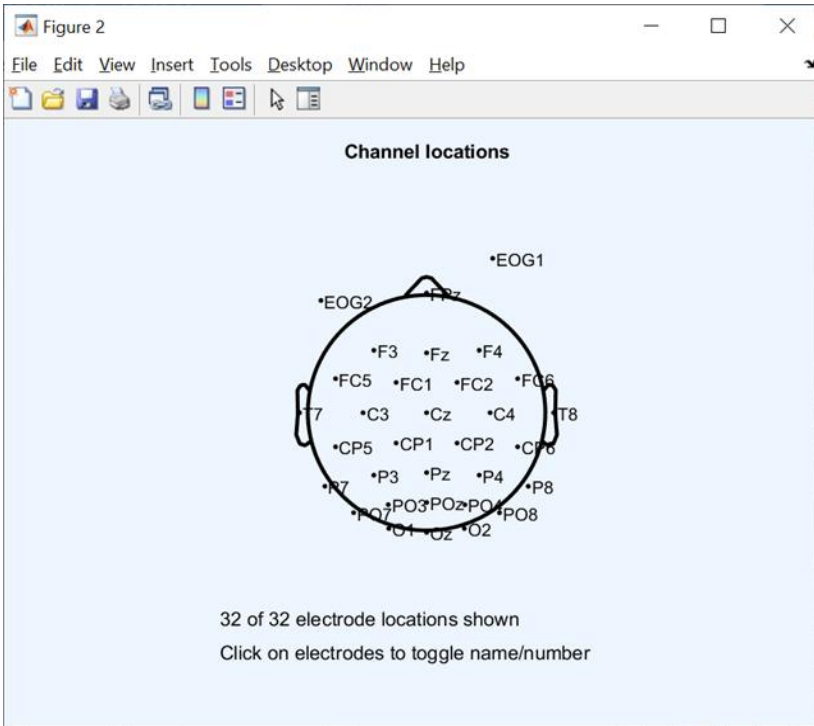


Figure 4.21: Advance Features: Electrode Placement

specific stimulus. These basic and advanced tools provided by EEGLAB allow for rapid and in-depth inspection and analysis of EEG data.

EEGLAB provides advanced tools for cleaning EEG data, including the "Clean RawData" and "Artifact Subspace Reconstruction (ASR)" methods. These tools are essential for removing noise and artifacts from EEG recordings, which can interfere with data analysis and interpretation. By using these tools, you can significantly improve the quality and reliability of your EEG data. To use the "Clean RawData" tool in EEGLAB, start by ensuring EEGLAB is running and your dataset is loaded. Navigate to the Tools menu, then select Reject data using Clean RawData. This will open a dialog box where you can configure parameters for data cleaning. The default settings are usually sufficient, but you can adjust them based on your dataset's specific

needs. Click OK to run the tool to process the data and remove segments with high noise levels or artifacts. Go to the Tools menu again for the Artifact Subspace Reconstruction (ASR) tool and select Reject data using ASR. In the dialog box that appears, configure the key parameters, such as the cutoff threshold, which determines the level of artifact removal, and the window length, which defines the length of data segments to be processed. After setting these parameters, click OK to run ASR. This tool will identify and correct artifacts by reconstructing the affected data segments. Both tools are integral for cleaning EEG data in EEGLAB, effectively removing noise and artifacts to enhance data quality. As shown in Fig. 4.22, the signals in red have been identified as potential rejects from the dataset.

**ERPs**

An Event-Related Potential (ERP) is a measured brain response directly resulting from a specific sensory, cognitive, or motor event. ERPs are derived

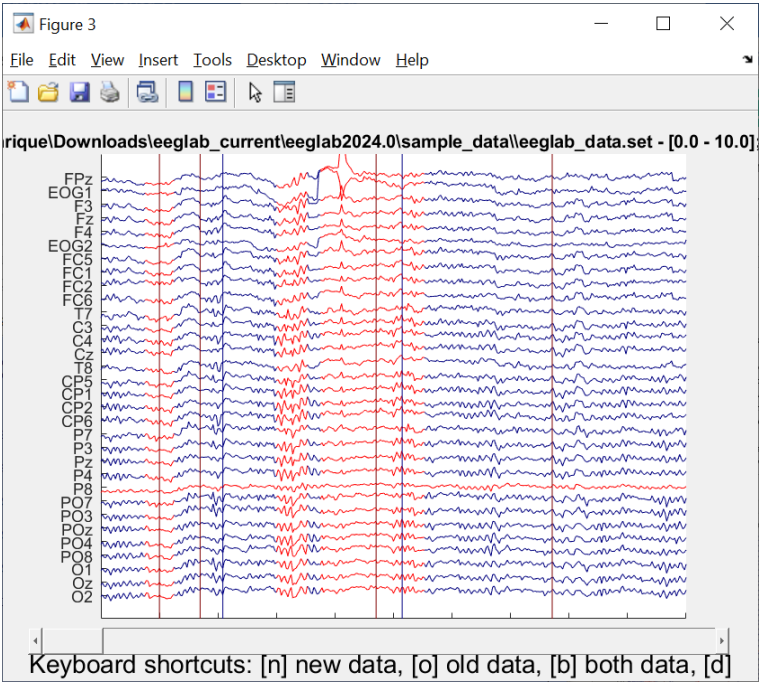


Figure 4.22: Cleaning EEG data

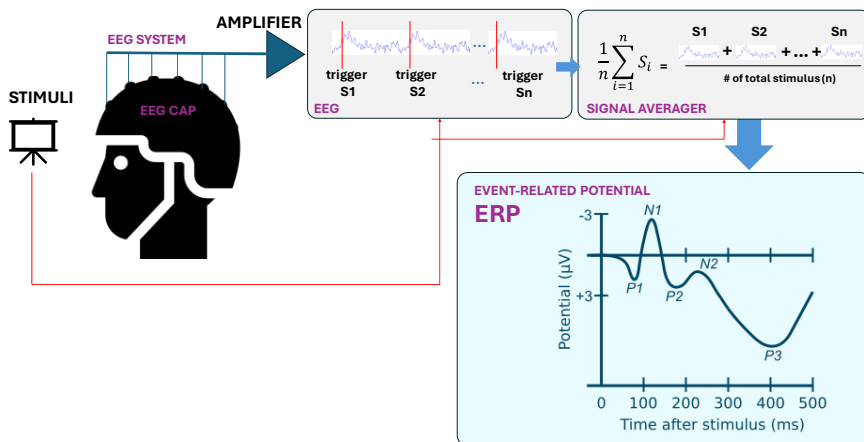


Figure 4.23: Event-related potential in response to a visual stimulus as obtained by averaging the EEG signal of multiple stimulus presentations (S1, S2,... Sn).

from electroencephalography (EEG) recordings and are used in cognitive neuroscience, psychology, and other fields to study brain function (Fig. 4.23 ).

### ***How ERPs are Obtained Based on EEG***

1. **EEG Recording** Electroencephalography (EEG) involves placing electrodes on the scalp to measure the electrical activity produced by neurons in the brain. The raw EEG signal is a complex mix of electrical activity from multiple sources, including both spontaneous brain activity and responses to specific events.
2. **Experimental Design** To obtain ERPs, researchers design experiments where participants are exposed to specific stimuli (e.g., visual, auditory, or tactile). These stimuli are presented at known times and often repeated to obtain reliable measurements.
3. **Time-Locking to Events** The EEG data is segmented into epochs, which are time-locked to the onset of the stimuli. Each epoch includes data from a short time window before and after the stimulus.
4. **Averaging** Because the EEG signal contains a lot of noise from unrelated brain activity, muscle movements, and external sources, individual epochs are averaged across many trials. This averaging

process helps to isolate the consistent brain response to the stimulus, as random noise tends to cancel out while the signal related to the event remains.

5. **Baseline Correction** Before averaging, a baseline correction is often performed. This involves subtracting the mean voltage of a pre-stimulus period (e.g., the time just before the stimulus is presented) from the entire epoch. This helps correct any slow drifts in the EEG signal.
6. **Resulting ERP Waveforms** The result of averaging and baseline correction is a series of ERP waveforms reflecting the brain's electrical response to the event. These waveforms consist of positive and negative voltage deflections (peaks and troughs) occurring at different latencies (times) after the stimulus.

### ***Key Components of ERPs***

- **Latency:** The time between the onset of the stimulus and the occurrence of a particular ERP component (peak or trough). This reflects the timing of neural processes.
- **Amplitude:** The magnitude of the voltage change associated with an ERP component can indicate the strength of the neural response.
- **Polarity:** Whether the ERP component is positive (upwards) or negative (downwards).
- **Topography:** The distribution of ERP amplitudes across the scalp can provide information about the source of the neural activity.

### ***Common ERP Components***

- **P300:** A positive deflection around 300 milliseconds after stimulus onset, often associated with attention and decision-making processes.
- **N400:** A negative deflection peaking around 400 milliseconds, related to language processing and semantic incongruence.
- **N170:** A negative component around 170 milliseconds, associated with face perception.

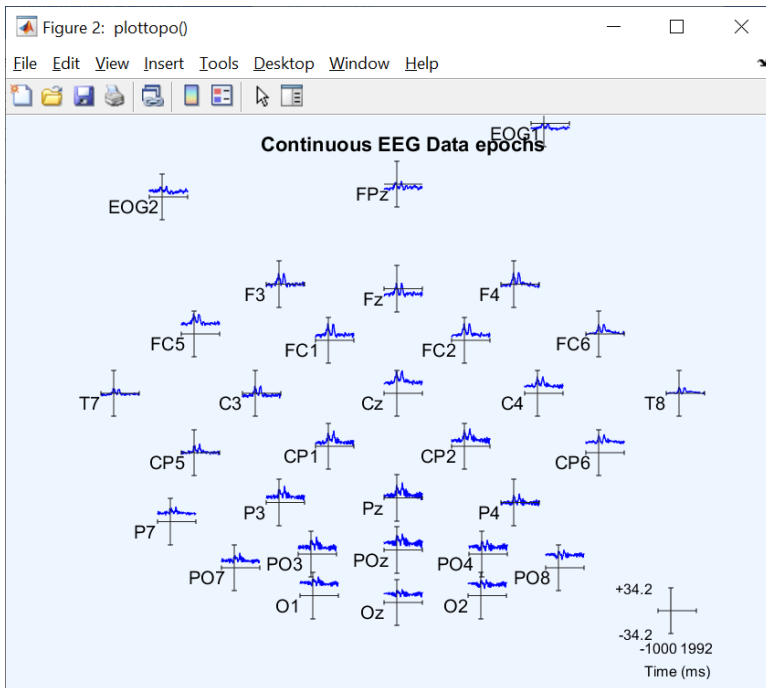


Figure 4.24: EEG Data Epochs

### ***Example of ERP Analysis Process***

1. Record EEG data while a participant performs a task involving repeated stimuli.
2. Segment the data into epochs around each stimulus presentation.
3. Apply baseline correction to each epoch.
4. Average the epochs to obtain the ERP waveform.
5. Analyze the ERP components to interpret the neural processes involved in the task. ERPs provide valuable insights into the timing and nature of cognitive processes by allowing researchers to examine the brain's electrical response to specific events in real-time. EEGLAB includes the extraction and examination of Event-Related Potentials (ERPs). To analyze ERPs using EEGLAB, researchers first import their raw EEG data into the software. They then preprocess the data,

typically involving filtering to remove noise, epoching the continuous EEG data into time segments around the events of interest, and performing baseline correction. Artifact rejection or correction methods are applied to remove noise from non-neural sources such as eye movements or muscle activity. Once clean epochs are obtained, they are averaged to isolate the ERP components related to specific stimuli or tasks. EEGLAB provides various tools for visualizing these ERP waveforms, including plotting the averaged ERP data and topographical maps to examine spatial distributions of the ERP components. Additionally, EEGLAB supports statistical analysis and comparison of ERP components across different experimental conditions. This comprehensive suite of tools within EEGLAB facilitates detailed ERP analysis, helping researchers interpret the neural mechanisms underlying cognitive processes.







## **Chapter 5**

### **Illuminating the Brain: Adventures with fMRI and fNIRS**

# Introduction and Learning Objectives

Leading up to this chapter, you will have learned about the anatomy and functions of the brain and its neurons. Neuroimaging techniques are critical tools that allow us to visualize these concepts in intriguing ways. Functional Magnetic Resonance Imaging (fMRI) and Near-Infrared Spectroscopy (fNIRS) are common methods. This chapter will explore these methods in detail and provide you with the information required to navigate and appreciate these tools within the field of engineering. By the end, you'll be able to understand the following:

- 1. Understand the principles of MRI, fMRI, NIRS, and fNIRS.*
- 2. Identify basic hardware components of the fMRI and fNIRS.*
- 3. Understand software tools used to process and analyze fMRI and fNIRS data*
- 4. Compare and contrast fMRI and fNIRS in terms of their applications in neuroengineering*
- 5. Apply knowledge of fMRI and fNIRS to practical neuroengineering laboratory exercises and research*

## Functional Magnetic Resonance Imaging (fMRI)

### *The Basics of MRI and fMRI*

At its core, MRI is a non-invasive neuroimaging technique that utilizes a large magnetic field along with radio waves to obtain a series of cross-sectional images of the brain (or any body part). Functional MRI builds on these principles by measuring changes in blood flow, specifically oxygenated blood, to visualize areas of increased brain activity. This approach, known as the Blood-Oxygen-Level Dependent (BOLD) signal, allows researchers to identify specific brain areas involved during various tasks [123].

For example, fMRI can show increased activity in the primary motor cortex when a subject performs a motor task, such as tapping their fingers. During a cognitive task, such as solving a complex math problem, fMRI could show

increased activity in the parietal lobe (and likely many other regions). Other interesting approaches to fMRI application involve the study of emotional responses, such as detecting heightened activity in the amygdala when viewing emotionally disturbing images.

By capturing changes in specific brain regions, fMRI can provide invaluable insight into the brain's functional organization. This allows researchers to map out our brain's vast network of connections. Projects such as the Human Connectome Project are working toward this initiative because researchers are motivated to improve our understanding of the brain. Now, we will discuss the finer details of how the fMRI process works.

### ***Magnetic Fields and Radio Waves***

Our bodies are full of water (H<sub>2</sub>O), especially for our brains. These hydrogen atoms play a crucial role in the function of the MRI. The magnet within an MRI has a strength of approximately ~1-3 tesla (T). In contrast, the earth's magnetic field is only around 0.00005 T. This MRI's intense magnetic field, called B<sub>0</sub>, interacts with the protons within hydrogen atoms in the body. Most of these hydrogen atoms are found in water molecules in the body. The intense magnetic field aligns most protons parallel to this magnetic field along the longitudinal axis. Some higher energy state protons align antiparallel to B<sub>0</sub> [124].

When the protons align with the magnetic field, they precess at the Larmor frequency rate. The Larmor frequency, or precession rate, is proportional to the strength, T, of the external magnetic field and is given by the equation:

$$\omega_0 = \gamma B_0 \quad (5.1)$$

Where  $\omega_0$  is the Larmor frequency,  $\gamma$  is the gyromagnetic ratio (specific to the type of nucleus, i.e., hydrogen proton), and B<sub>0</sub> is the strength of the magnetic field [125].

Subsequently, a radiofrequency (RF) pulse is applied at a frequency equivalent to the Larmor frequency. This RF pulse provides electromagnetic energy to the protons, exciting them to a high-energy state. The net magnetization vector

aligns perpendicular to  $B_0$  along the transverse plane when the protons are placed into this high-energy state. This process is commonly referred to as excitation. As the protons return to their low energy state and the net magnetization vector realigns with the magnetic field  $B_0$ , the protons emit radio signals [126]. These radio signals are detected and used to form the images we see of the brain.

This complex interaction between magnetic fields, radio waves, and the water within our bodies allows the MRI to produce detailed images of the body's internal structures.

### ***T1 and T2 Relaxation Times***

There are two primary measurement parameters of the MRI: T1 and T2 relaxation time constants. As discussed previously, the protons of mainly water molecules are aligned to the magnetic field and then energized into the transverse plane by the radiofrequency pulse. The T1 relaxation time constant measures the time it takes for protons to realign with the MRI's magnetic field  $B_0$  following the radiofrequency pulse. You may also see this as longitudinal relaxation or spin-lattice relaxation time. The T2 relaxation time constant is when the protons lose phase coherence with each other in the transverse plane[127]. This is commonly called spin-spin relaxation or transverse relaxation time.

These two-time constants are important for the generation of the brain images that you see from an MRI. Images are commonly denoted as T1 or T2 weighted, which will influence the contrast of various tissues in the brain. T1 weighted images are useful for visualizing detailed brain anatomy. T2 weighted images are useful for identifying pathological changes.

### ***Blood-Oxygen-Level Dependent (BOLD) Signal***

Now that we have a general understanding of how MRI functions, we can focus specifically on the application of fMRI. The key aspect of fMRI is the blood-oxygen-level dependent, or BOLD, signal. When neurons are active, they require and consume more oxygen. The body accomplishes this demand by increasing blood flow to the active neurons to deliver more oxygenated blood. Oxygenated blood has different magnetic properties from deoxygenated

blood. Specifically, oxygenated blood is diamagnetic, which means it repels magnetic fields, whereas deoxygenated blood is paramagnetic, which means it attracts magnetic fields. These differences, measured as the BOLD signal, produce a map of brain activity.

As neuronal activity changes in a specific region, the proportion of oxygenated to deoxygenated blood changes, resulting in local measurable changes in the magnetic field. This resultant BOLD signal is technically an indirect measure of neuronal activity, reflecting the hemodynamic response to neural activation [123]. One advantage of the BOLD signal is the ability to provide high spatial resolution images in the 1-3 millimeters range. However, the BOLD response is delayed by several seconds due to the time it takes for the blood flow to increase in response to neural activity. This delay limits the temporal resolution of fMRI.

## ***Hardware Components of MRI***

There are three primary hardware components that you should familiarize yourself with:

### ***Magnets***

The primary magnet creates a strong magnetic field,  $B_0$ . This magnet is typically a superconducting magnet cooled to very low temperatures using liquid helium. The strength of this magnet is measured in teslas (T), with clinical MRI machines typically operating at 1.5 – 3 T.

### ***Gradient Coils***

These coils are responsible for the spatial encoding of the MR signal. They create small, linear variations in the magnetic field in the X, Y, and Z directions. This allows for the localization of the MR signal and the construction of images in different planes.

### ***RF Coils***

The RF coils transmit the RF pulses that excite the protons. The RF coils are also used to receive the signals emitted by the protons as they relax.



Figure 5.1: An MRI scanner [128]

An MRI scanner is shown in Fig. 5.1 [128]. The large cylindrical structure contains the primary magnets that generate the  $B_0$  field. The remaining hardware components are not visible in the image.

### ***Software for fMRI***

The processing and analysis of fMRI data is crucial for performing research and interpreting information. Two commonly used open-source software for pre-processing and post-processing fMRI data are FMRIB Software Library (FSL) and FreeSurfer [129], [130][7]. FSL is an open-source library of tools capable of performing in-depth analysis of fMRI data. It was created by “The Analysis Group” at the University of Oxford. FSL also offers tools for analyzing resting-state fMRI data, allowing researchers to study functional connectivity across different brain regions. Its user-friendly interface and comprehensive documentation make it accessible to researchers at all levels.

FreeSurfer is a similar software that the Laboratory developed for Computational Neuroimaging at the Athinoula A. Martinos Center for Biomedical Imaging. It is renowned for its capabilities in cortical surface reconstruction and volumetric segmentation. FreeSurfer's tools can accurately segment the brain into different regions of interest, providing detailed anatomical maps. Additionally, FreeSurfer excels in measuring cortical thickness and surface area, which are valuable metrics in studies of brain development and neurodegenerative diseases.

These tools follow similar workflows for processing fMRI data. This includes preprocessing, registration (alignment), segmentation, statistical analysis, and visualization. These tools offer abundant guides and resources that are freely available online. By leveraging these tools, you can conduct unique experiments that contribute to our understanding of the brain's workings.

## ***Experimental Design***

Designing an fMRI experiment involves careful planning to ensure that the data collected can answer the research question. Key elements include task design, control conditions, and timing.

### ***Task Design***

Task design is a critical element in fMRI experimental design, as it directly influences the brain activity that will be measured and analyzed. The tasks or stimuli presented to participants are carefully crafted to engage specific cognitive, sensory, or emotional processes, allowing researchers to investigate the neural underpinnings of these functions.

### **Customization of Tasks to Research Questions**

The specific nature of the tasks used in an fMRI experiment highly depends on the research question being addressed. Researchers must design tasks that effectively target the brain regions or cognitive processes of interest. This customization ensures that the observed brain activity is directly related to the studied phenomenon. There are several different task types, such as:

### *Cognitive Tasks*

These tasks engage mental processes such as memory, attention, language, problem-solving, or decision-making. For instance, in a study investigating working memory, participants might be asked to keep a series of numbers or letters in mind and manipulate them mentally, such as by reversing their order. The brain activity during this task would primarily involve regions associated with working memory, like the prefrontal cortex.

### *Language Processing Tasks*

To study language processing, tasks might involve reading sentences, listening to spoken words, or generating speech. For example, participants could be asked to read sentences that vary in syntactic complexity, allowing researchers to examine how different brain areas contribute to understanding and processing language.

### *Decision-Making Tasks*

Decision-making tasks often involve presenting participants with choices that require evaluation and selection based on certain criteria, such as risk, reward, or moral judgment. These tasks can activate brain regions involved in executive functions, such as the prefrontal cortex and the anterior cingulate cortex.

### *Emotional Processing Tasks*

Emotional tasks are designed to elicit specific emotional responses. For example, participants might be shown images or videos that are sad, happy, or frightening. The resulting brain activity, particularly in regions like the amygdala and orbitofrontal cortex, can provide insights into how emotions are processed and regulated.

### **Considerations in Task Complexity**

The complexity of the task is a crucial factor in fMRI experimental design. Tasks must be engaging enough to activate the brain regions of interest but not so difficult that they lead to participant frustration or disengagement, which could negatively impact the data quality. Researchers should consider the following when thinking about task complexity.

### *Task Engagement*

An engaging task ensures that participants are fully involved, which increases the likelihood of eliciting robust brain activity. For example, if the task is too simple, participants may not exert enough mental effort, resulting in minimal activation in the target brain areas. Conversely, if the task is overly complex, participants may become overwhelmed, leading to variable performance and potential artifacts in the data.

### *Pilot Testing*

Before the actual fMRI study, tasks are often pilot-tested with a small group of participants. This helps fine-tune the difficulty level, ensuring it is appropriate for the study population. Pilot testing can also identify task instructions or timing issues that could affect data quality.

### *Task Timing and Duration*

The timing and duration of the task are also critical considerations. Tasks are typically organized into blocks or trials, with specific intervals between stimuli presentations to allow the brain to respond and recover. The duration of each task block or trial should be carefully calibrated to ensure that the fMRI scanner can reliably capture the brain activity. A duration that is too short may not allow for sufficient signal accumulation, while too long could lead to participant fatigue.

### *Example: Memory Recall Task*

Participants might be shown images or words during an initial encoding phase in a memory recall task. After a delay, they are asked to recall or recognize these items during retrieval. The brain activity during both the encoding and retrieval phases can be measured, allowing researchers to examine the neural mechanisms underlying memory formation and recall. During the encoding phase, participants are exposed to stimuli (e.g., images, words) and are instructed to memorize them. This phase activates brain regions involved in memory formation, such as the hippocampus and the medial temporal lobe. In the retrieval phase, participants are asked to recall or recognize the previously presented stimuli. This phase engages regions involved in memory retrieval, such as the prefrontal cortex and parietal lobes. Comparing brain activity

between successful and unsuccessful recalls can provide insights into the processes that facilitate or hinder memory retrieval.

### Impact on Data Quality

The task design directly impacts the quality of the data collected during an fMRI experiment. Poorly designed tasks can lead to uninterpretable or confounded results. For example, if a task is too difficult, participants may fail to engage in the intended cognitive processes, resulting in weak or inconsistent brain activation patterns. Additionally, high variability in task performance across participants can introduce noise into the data, making it challenging to detect the true neural correlates of the task.

In summary, task design is a fundamental aspect of fMRI experimental design that requires careful consideration of the research question, task complexity, and participant engagement. The task must be precisely tailored to elicit the desired brain activity while maintaining a difficulty appropriate for the study population. Proper task design, often refined through pilot testing, is essential for obtaining reliable and meaningful data in fMRI studies.

### ***Control Conditions***

Control conditions are essential in neuroimaging experiments as they allow researchers to differentiate the brain activity related to the experimental task from unrelated or background activities. The careful design of control conditions ensures that the observed changes in brain activity can be attributed to the specific cognitive or emotional processes being studied rather than to general factors such as attention, sensory processing, or motor responses. Different control conditions exist, such as resting-state scans and baseline tasks.

### Resting-State Scans

In resting-state scans, participants are instructed to relax and avoid engaging in specific mental tasks. This condition is a baseline for measuring the brain's intrinsic activity without external stimuli or cognitive demands. Resting-state data can reveal the brain's default mode network, which is active when the brain is at rest and not focused on the outside world. Comparing task-related brain activity to this baseline helps isolate the neural responses specifically elicited by the experimental stimuli.

## Baseline Tasks

Baseline tasks are designed to be similar to the experimental task but lack the critical component under investigation. This design helps control for non-specific factors such as visual or auditory processing, attention, or motor activity that might otherwise confound the results. For instance, in a study investigating the brain's response to emotional stimuli, a baseline task might involve viewing neutral images similar in visual complexity to those used in the experimental condition. This approach allows us to subtract the brain activity associated with general visual processing, leaving behind the activity specifically related to emotional processing.

### Example: Emotional Processing Experiment

Consider an experiment designed to investigate how the brain processes emotional stimuli. In the experimental condition, participants might be shown emotionally charged images, such as pictures of sad, happy, or fearful faces. These images will likely elicit strong emotional responses, engaging brain regions involved in emotion regulation, such as the amygdala, prefrontal cortex, and other limbic system areas. A carefully designed control condition is necessary to isolate the brain regions involved in emotional processing. In this case, the control condition might involve showing participants neutral images, such as pictures of ordinary objects or faces with neutral expressions. These images should be visually like the emotional stimuli in terms of complexity, brightness, and other visual features but should not evoke a strong emotional response.

By comparing brain activity during the experimental condition (emotional images) with the control condition (neutral images), researchers can identify the brain regions specifically activated by emotional processing. This comparison helps to eliminate the confounding effects of general visual processing, attention, or other non-emotional factors, ensuring that the observed activity is truly related to the emotional content of the stimuli.

### Importance of Control Conditions in Data Interpretation

Control conditions are crucial for accurate data interpretation in these experiments. Without appropriate control conditions, it would be challenging to

determine whether the observed brain activity is truly related to the cognitive or emotional processes of interest or simply a result of unrelated factors.

Moreover, using well-designed control conditions allows for more precise localization of brain function. By subtracting the activity observed during the control condition from that observed during the experimental condition, researchers can create a "difference map" highlighting the regions specifically involved in the task. This approach enhances data's spatial and functional resolution, leading to more reliable and meaningful conclusions about brain function.

In summary, control conditions are an indispensable part of experimental design in imaging studies. They allow researchers to isolate the brain activity associated with the specific cognitive or emotional processes under investigation, ensuring that the results accurately reflect the neural mechanisms at play.

### ***Timing***

The timing of stimuli presentation and task execution in fMRI experiments is critical because the BOLD response, which fMRI measures, is not instantaneous. The BOLD response reflects changes in blood flow and oxygenation levels in the brain that occur in response to neural activity. This response is delayed, typically peaking about 5-6 seconds after the initial neural activity and slowly returning to baseline. Therefore, precise control over the timing of stimuli and tasks is necessary to accurately correlate these with the BOLD signal and ensure that the collected data reflects the underlying neural processes. Different types of experimental designs can be used to control the timing of stimulus, such as Event Related Design and Block Design.

### ***Event-Related Design***

An event-related design in fMRI experiments involves presenting individual stimuli or tasks at specific intervals, with each event being isolated in time. This design allows researchers to examine the brain's response to each stimulus separately, providing detailed information about transient neural processes. The event-related design offers high temporal resolution, allowing for the detection of neural responses to discrete events. Each stimulus is typically followed by a rest period or another stimulus, allowing researchers to observe

how the BOLD response evolves for each event. This design is also particularly useful for studying cognitive processes that occur over a short duration, such as decision-making, error processing, or rapid sensory perception. By analyzing the BOLD response to each event, researchers can investigate the timing and sequence of brain activation across different regions. To prevent participants from anticipating stimuli, which could lead to confounding effects, the timing of stimuli presentation is often randomized or "jittered" (i.e., small variations in the timing of stimuli presentation are introduced). This approach helps to disentangle the neural responses to different stimuli and improves the statistical power of the analysis.

### Block Design

In a block design, stimuli or tasks are presented in continuous blocks of time, alternated with rest or control blocks. This approach effectively detects sustained brain activity over time and is particularly useful for studying processes requiring sustained attention or involving continuous cognitive engagement. Block designs typically have a higher signal-to-noise ratio compared to event-related designs. This is because the sustained nature of the task during each block leads to a more pronounced and stable BOLD response. By averaging the BOLD response throughout the block, researchers can enhance the detection of neural activity related to the task. Block designs are often used in studies of sustained cognitive processes, such as language processing, motor tasks, or emotional regulation. For instance, in a study examining language processing, participants might be asked to read words aloud during the experimental blocks and view meaningless symbols during the control blocks. Researchers can identify the brain regions involved in language processing by comparing the BOLD responses during the experimental and control blocks. The alternating pattern of task and rest/control blocks allows researchers to compare brain activity across different conditions, such as experimental versus control or various types of stimuli. This comparison is crucial for isolating the specific neural correlates of the task or stimuli being studied.

## Considerations for fMRI Experimental Design

In addition to the choice of event-related or block design, several other factors must be carefully considered to ensure the success of an fMRI experiment:

### *Duration of the Scan Session:*

The length of the scan session should be carefully planned to balance the need for sufficient data with participant comfort and attention. Scan sessions that are too long can lead to participant fatigue, boredom, or discomfort, which can introduce noise into the data. Shorter, well-structured sessions with adequate breaks can help maintain participant engagement and data quality.

### *Number of Trials or Blocks:*

The number of trials (in an event-related design) or blocks (in a block design) should be sufficient to provide robust data for statistical analysis. A higher number of trials or blocks increases the reliability of the results by allowing for the averaging of multiple BOLD responses, which reduces the impact of random fluctuations in the data. However, this must be balanced against the potential for participant fatigue.

### *Participant Instructions:*

Clear and concise instructions are essential to ensure participants understand and consistently perform the task throughout the scan. Inadequate or confusing instructions can lead to variability in task performance, which can confound the results. Practice sessions outside the scanner can be useful for familiarizing participants with the task before the scan.

### *Minimizing Motion Artifacts:*

Motion artifacts are a significant concern in fMRI studies, as even small movements can lead to distortions in the BOLD signal. Participants should be instructed to remain as still as possible during the scan to minimize motion. Comfortable padding and head restraints are often used to reduce involuntary movements. Additionally, real-time motion correction techniques can be applied during data acquisition and analysis to further minimize the impact of motion artifacts.

### Stimulus Presentation and Timing:

The precise timing of stimulus presentation is crucial for correlating it with the BOLD response. This requires accurate synchronization between the fMRI scanner and the stimulus delivery system. Any delays or inaccuracies in timing can lead to misalignment between the task and the measured brain activity, compromising the validity of the results.

### Practical Example: Language Processing Study

Let's consider an example of a study on language processing. In such a study, participants might be asked to read words aloud during experimental blocks and view meaningless symbols during control blocks. The experiment could be designed as follows:

#### *Block Design*

Participants alternate between blocks of reading words (experimental condition) and blocks of viewing symbols (control condition). Each block might last 20-30 seconds, followed by a rest period.

#### *Task Timing*

The presentation of each word or symbol within the block is precisely timed, with a fixed interval between stimuli to allow for consistent BOLD responses.

#### *Control Blocks*

The control blocks with meaningless symbols help isolate the brain activity related to language processing, as the control condition engages similar sensory and motor processes without involving language comprehension.

#### *Analysis*

By comparing the BOLD response during the experimental and control blocks, researchers can identify brain regions, such as Broca's and Wernicke's areas, that are specifically activated during language processing.

In summary, the timing and design of stimuli presentation and task execution in fMRI experiments are critical for accurately measuring the BOLD response and drawing meaningful conclusions about brain activity. Event-related and block designs each have their strengths and are chosen based on the nature of the cognitive processes being studied. Alongside these considerations, careful attention to scan duration, trial/block numbers, participant instructions, and

motion artifact reduction is essential for ensuring the quality and reliability of the data.

### ***Advantages and Disadvantages***

The main advantage behind fMRI use is that it is a non-invasive imaging technique. Additionally, fMRI is advantageous for its high spatial resolution, allowing for the precise localization of brain activity, typically 2-3 millimeters. This allows for mapping brain region activity when performing the specific functional tasks employed by the experimental design.

A major disadvantage of the fMRI is that it has low temporal resolution. It does not effectively capture rapid changes in brain activity during tasks. The fMRI is also sensitive to artifacts, which can be introduced by motion and magnetic interference.

## **Functional Near-Infrared Spectroscopy (fNIRS)**

### ***The Basics of NIRS and fNIRS***

Functional Near-Infrared Spectroscopy (fNIRS) is another non-invasive imaging technique that measures brain activity by detecting changes in blood oxygenation. fNIRS uses near-infrared light to penetrate the skull and measure light absorption by oxygenated and deoxygenated hemoglobin. This allows researchers to infer brain activity based on changes in blood oxygen levels.

### ***Infrared Light***

Functional Near-Infrared Spectroscopy (fNIRS) utilizes near-infrared light, which can penetrate biological tissues and reach the brain's surface. This light typically ranges from 650 to 900 nanometers. The key to fNIRS is how this light interacts with hemoglobin in the blood. Hemoglobin exists in two forms:

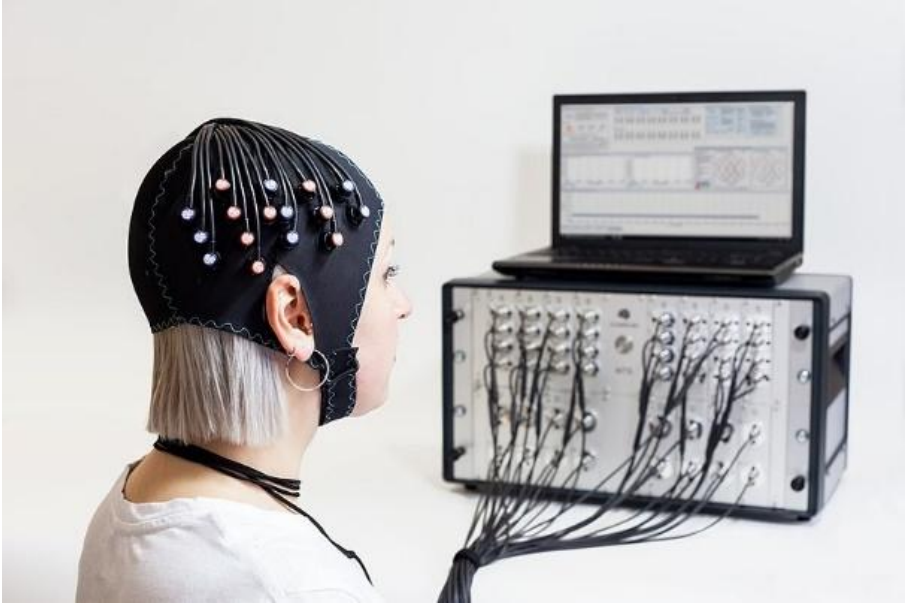


Figure 5.2: An fNIRS device worn on the head and hardware components [131]

oxygenated (HbO) and deoxygenated (HbR). These two forms absorb near-infrared light differently, providing a way to measure changes in blood oxygenation.

Oxygenated hemoglobin primarily absorbs light at around 850 nanometers, while deoxygenated hemoglobin absorbs more light at around 760 nanometers. These differences in absorption arise from the molecular structure of hemoglobin, which changes depending on whether it is bound to oxygen. The absorption properties of HbO and HbR can be attributed to the iron-containing heme groups within the hemoglobin molecules. When hemoglobin binds to oxygen, the electronic structure of the heme group is altered, which in turn affects how the molecule interacts with light. This interaction results in different absorption patterns for HbO and HbR, making it possible to distinguish between them using near-infrared light [130].

Detectors placed on the scalp measure the intensity of the light that is either transmitted through or reflected from the brain tissue. By analyzing light absorption at the wavelengths corresponding to HbO and HbR, fNIRS can

determine the relative concentrations of these two forms of hemoglobin. The principles of fMRI hold for fNIRS, wherein brain regions that become more active consume more oxygen.

The ability of near-infrared light to differentiate between oxygenated and deoxygenated hemoglobin forms the foundation of fNIRS. This non-invasive and portable technique provides valuable insights into brain function. Researchers can use fNIRS to study brain activity during various cognitive tasks, motor activities, and other functional processes in multiple environments and applications.

### ***Hardware Components of fNIRS***

The primary hardware components of an fNIRS system are shown in Fig. 5.2 [131] and include:

#### ***Light Sources***

Near-infrared light emitters that illuminate the scalp.

#### ***Detectors***

Sensors that detect the light after it has passed through the brain tissue.

#### ***Optodes***

Light sources and detectors are combined on the scalp to measure the hemodynamic response.

### ***Software for fNIRS***

Two common open-source software tools are used to process and analyze fNIRS data: Homer3 and NIRS-SPM[132], [133]. Both tools take advantage of the MATLAB platform. Homer3 is a software that the Boston University Neurophotonics Center developed. NIRS-SPM is a software package developed by the Bio-Imaging Signal Processing lab at KAIST in Korea. These tools allow for importing and pre-processing fNIRS data through filtering and motion correction. The statistical analysis performed by these software tools is commonly the General Linear Model (GLM), which determines the significance of observed changes in hemoglobin concentrations. Finally, these software provide their means for visualizing the

results. Like the fMRI software discussed, both tools have many resources available for free online.

## ***Experimental Design***

Designing an fNIRS experiment involves:

### ***Task Design***

Like fMRI, participants perform tasks or are exposed to stimuli to elicit brain activity. These tasks are designed to engage cognitive, sensory, or motor functions, which in turn activate specific regions of the brain. The task choice depends on the research question and brain regions of interest. There are different types of tasks, such as cognitive (working memory and problem-solving tasks), motor (finger tapping and hand movements), or sensory (visual or auditory stimuli). For example, a working memory task would be employed in research to study prefrontal cortex activity.

### ***Placement of Optodes***

Careful placement of light sources and detectors on the scalp ensures accurate hemodynamic response measurement. Optodes are typically placed according to the 10-20 system (Chapter 4). This system helps ensure that optodes are positioned over specific cortical areas corresponding to the brain regions of interest. The distance between the source and detector optodes is typically between 2.5 and 4 cm. This distance is optimal for measuring the hemodynamic response from the brain's cortical layer. If the distance is too short, the signal may be dominated by superficial tissue, while a distance that is too long may result in signal loss or contamination by deeper structures. The configuration of optodes (the pattern in which they are placed on the scalp) is also important. The configuration can vary depending on the area of the brain being studied. For example, optodes might be arranged in a dense array over the forehead if the study focuses on the frontal cortex. The arrangement can also be multi-channel, covering large areas of the scalp for whole-brain measurement.

## ***Control Conditions***

Used to isolate the brain activity related to the task from other sources of variability and are like that of fMRI. The unique aspects of fNIRS, including its sensitivity to changes in blood oxygenation and its non-invasive nature, make the design of control conditions, particularly important and include additional controls that researchers should consider, such as the following:

### **Physiological Noise Control**

fNIRS is sensitive to physiological signals such as heart rate, respiration, and blood pressure, which can introduce noise into the data. Control conditions are designed to differentiate task-related brain activity from these physiological signals. For instance, during a resting baseline condition, participants might be asked to sit quietly without engaging in cognitive tasks. This allows researchers to measure the baseline hemodynamic response associated with resting physiology, which can then be subtracted from the task-related signals.

### **Superficial Tissue Signal Isolation**

fNIRS measures changes in light absorption related to blood oxygenation in both the brain and superficial tissues like the scalp. Control conditions help isolate the signals originating from the brain by accounting for the superficial tissue responses. For example, in a task involving head movement, a control condition might involve the same movement without the cognitive task, allowing for identifying and subtracting movement-related artifacts.

### **Ambient Light and Environmental Factors**

External factors such as ambient light or temperature changes can affect fNIRS measurements. Control conditions that match the environmental conditions of the experimental task but without cognitive or sensory stimulation help to identify and control for these external influences. This ensures that the observed brain activity is not confounded by environmental variability.

### **Temporal Dynamics Control**

The hemodynamic response measured by fNIRS is inherently dynamic, with changes occurring over time as the brain processes stimuli. Control conditions that involve time-matched tasks without the specific cognitive demand help

distinguish between the time-related changes in brain activity due to the task and those that occur naturally or due to other factors. This can be particularly important in functions that involve learning or adaptation over time, where brain activity might change as the participant becomes more familiar with the task.

### Cognitive Load Control

fNIRS is often used to study tasks involving varying cognitive load levels. Control conditions with different levels of cognitive load, such as a simple task compared to a more complex one, help isolate the specific brain regions and responses associated with increased cognitive demands. This approach allows researchers to understand better how cognitive load influences brain activity and to separate these effects from other factors.

### *Advantages and Disadvantages*

Like fMRI, fNIRS is a highly advantageous non-invasive imaging technique. Its key strengths include portability and ease of use, which enable fNIRS experiments to be conducted in a wide range of environments—from traditional laboratory settings to more naturalistic or mobile conditions. This versatility makes fNIRS particularly valuable for studies that require flexibility and real-world applicability. Moreover, fNIRS offers excellent temporal resolution and can measure changes in brain activity in hundreds of milliseconds. This high temporal resolution allows researchers to capture rapid fluctuations in neural activity, which is essential for understanding dynamic brain processes and cognitive functions.

Despite these advantages, fNIRS has notable limitations, primarily related to its spatial resolution and depth sensitivity. The spatial resolution of fNIRS is constrained to approximately 1-3 cm, which limits its ability to localize brain activity to smaller or closely spaced regions precisely. This lower spatial resolution means that fNIRS is less effective for tasks that require fine-grained anatomical detail. Additionally, the depth sensitivity of fNIRS is limited to around 1-3 cm beneath the cortical surface, which restricts its capacity to detect activity in deeper brain structures. This limitation poses challenges for

studying subcortical regions and understanding their roles in various neural processes.

Efforts are underway to address some of these limitations, particularly by developing multichannel NIRS systems. These advanced systems aim to improve spatial resolution by increasing the number of measurement channels and enhancing the sensitivity to different depths. While these advancements hold promise for overcoming some of the current constraints of fNIRS, they are still in the developmental stages and have not yet fully realized the potential improvements. Future enhancements in fNIRS may offer better spatial and depth resolution as research and technology evolve, expanding its applicability and effectiveness in neuroimaging studies.

## **Comparing fMRI and fNIRS**

Both functional imaging techniques, fMRI and fNIRS, have distinct strengths and weaknesses that make them suitable for different research questions and settings. fMRI excels in providing high spatial resolution, allowing for detailed brain activity mapping with precise localization of neural processes. This high spatial resolution is particularly advantageous for studies that require an in-depth understanding of the anatomical specificity of brain functions and the accurate identification of neural networks involved in complex cognitive tasks. However, fMRI has limitations in temporal resolution, which means it is less effective at capturing the rapid fluctuations in brain activity over time. Additionally, fMRI is significantly more expensive and less portable than fNIRS, often requiring participants to remain still in a large, stationary machine, which can limit its applicability in more dynamic or naturalistic environments.

On the other hand, fNIRS provides excellent temporal resolution, making it well-suited for capturing rapid changes in brain activity with a finer temporal granularity. This capability is crucial for understanding how brain activity evolves over short periods and studying processes that occur on a millisecond scale. Moreover, fNIRS is more portable and less expensive than fMRI, allowing for greater flexibility in experimental design and the possibility of studying participants in more naturalistic settings. This portability and ease of

use make fNIRS particularly valuable for research involving young children, individuals with movement disorders, or studies that require mobile or ecologically valid conditions. However, fNIRS has limitations in spatial resolution, which means it is less effective at pinpointing the exact locations of brain activity and is generally less capable of differentiating between closely spaced brain regions.

Ultimately, the choice between fMRI and fNIRS depends on the specific research objectives and the nature of the experimental conditions. Researchers must weigh the importance of spatial versus temporal resolution and practical considerations such as cost and the study setting to determine the most appropriate imaging technique for their needs.

## **Ethical Considerations**

Several considerations should be considered when conducting research using fMRI and fNIRS to ensure the study is conducted responsibly. Both fMRI and fNIRS involve collecting neuroimaging data, which can raise concerns about participants' privacy and data security. Researchers must obtain informed consent that clearly explains the nature of the study, the procedures, and any potential risks or benefits. Additionally, researchers should ensure that participants have the autonomy and right to withdraw from the study at any time with no consequences. Data must be handled strictly to protect participants' identities and personal information. The potential for unexpected results that could have clinical implications requires careful consideration, and participants should be informed about how these findings will be managed and communicated. Furthermore, researchers should be mindful of their findings' impact on individuals and groups and avoid potential data misuse that could lead to stigmatization or discrimination. Researchers should maintain transparency, respect participants' rights, and ensure data integrity when conducting fMRI and fNIRS research.

## **Chapter 5: Summary**

In conclusion, fMRI and fNIRS are powerful neuroimaging techniques that provide complementary insights into brain function. By understanding these

methods' principles, hardware, software, advantages, and disadvantages, researchers can effectively apply them in neuroengineering research. Each technique offers unique strengths—fMRI, with its high spatial resolution for detailed brain mapping, and fNIRS, which has excellent temporal resolution and portability for dynamic and naturalistic studies. Leveraging these strengths allows researchers to understand brain activity and its underlying mechanisms comprehensively.

As you continue your exploration through this book and your research endeavors, I encourage you to apply these concepts and techniques to your experiments. Consider developing a novel fMRI experimental design to reveal new intricacies within the brain or analyze and interpret fNIRS data from previous research to uncover fresh insights. Given the knowledge and resources you now possess regarding fMRI and fNIRS, these challenges are well within your capabilities. Your ability to make meaningful contributions to the broader field of neuroengineering is within reach.

The next adventure in your research journey will involve integrating what you have learned about neuroimaging techniques with exploring brain-computer interfaces (BCIs). BCIs represent a cutting-edge area of research that bridges the gap between neural activity and external devices, enabling direct communication between the brain and technology. In the upcoming chapters, you will build on your understanding of fMRI and fNIRS to delve into the design, implementation, and application of BCIs. This new domain will challenge you to apply your neuroimaging insights innovatively, potentially transforming how we interact with and understand the brain. Prepare to embark on this exciting frontier, where your skills and knowledge will contribute to pioneering advances in neuroengineering and beyond.



# Chapter 5: Learning Activities

## Learning Activity 5.1

Task: take 10 minutes to find online available images of fMRI



### *Objective*

Students will search for and analyze functional Magnetic Resonance Imaging (fMRI) images to understand their applications and interpretations in neuroengineering.

### *Materials*

- Internet access
- Computers or tablets
- Note-taking materials (paper, pens, or digital tools)

### *Time*

10 minutes

### *Instructions*

Step 1. Introduction (2 minutes): Start by explaining the purpose of the activity. I.e., "Today, we are going to explore fMRI images. Functional MRI is a crucial tool in neuroengineering that helps us understand brain activity by measuring changes in blood flow." "Your task is to find online images of fMRI scans. You will have 10 minutes to find and download these images."

Step 2. Searching for fMRI Images (6 minutes): Allow students to begin their search.

Step 3. Sharing and Discussion (1 minute): Gather the students' attention once the time is up.

Step 4. Analysis and Reflection (5 minutes): Facilitate a brief discussion about the images. I.e.

- "Who would like to share an image they found? Describe what you see in the fMRI scan and any interesting details."

- "What tasks or stimuli do you think caused the brain activity shown in the image?"
- "How might these images be useful in neuroengineering research or clinical practice?"

Step 5. Summarize the key takeaways from the activity.

Follow-up Assignment: (Optional) Assign a follow-up activity where students write a short report on one of the fMRI images they found, including its source, the activated brain regions, and potential neuroengineering applications.

## Learning Activity 5.2

### *Objective*

Students will engage in a problem-based learning activity to brainstorm and propose innovative solutions to reduce the cost of fMRI (functional Magnetic Resonance Imaging).



### *Materials*

- Whiteboard or flip chart
- Markers
- Internet access
- Computers or tablets
- Note-taking materials (paper, pens, or digital tools)

### *Time*

30-45 minutes

### *Instructions*

#### *Introduction (5 minutes):*

1. Introduce the challenge and provide context about the high cost of fMRI and its importance in neuroengineering.

2. Explain the goal of brainstorming and proposing solutions to make fMRI more affordable.

***Group Formation (2 minutes):***

3. Divide the class into small groups of 3-4 students.

***Problem Exploration (5 minutes):***

4. Instruct each group to discuss the factors contributing to the high cost of fMRI, such as equipment, maintenance, personnel, and operational expenses.

***Research and Brainstorming (15 minutes):***

5. Guide the groups to research and brainstorm potential solutions to reduce the cost. Encourage them to think creatively and consider:
  - Technological advancements
  - Alternative imaging methods
  - Cost-cutting measures
  - Innovative funding strategies

***Solution Development (10 minutes):***

6. Ask each group to choose and develop the most promising ideas into a coherent proposal.
7. Have the groups prepare a brief presentation to share their solutions with the class.

***Presentation and Discussion (10 minutes):***

8. Facilitate the presentations, allowing each group 2 minutes to present their ideas.
9. Lead a discussion on the feasibility and potential impact of the proposed solutions.

***Conclusion (3 minutes):***

10. Summarize the activity and highlight key takeaways, emphasizing the importance of innovative and collaborative problem-solving in neuroengineering.
-

## Learning Activity 5.3

### *Activity: Buzz Groups and Pugh Chart Analysis - Comparing Brain Imaging Techniques*



#### ***Objective***

Students will collaborate in small (buzz) groups to compare different brain imaging techniques (fMRI, fNIRS, EEG, MEG) and create a Pugh chart to evaluate their advantages and disadvantages.

#### ***Materials***

- Whiteboard or flip chart
- Markers
- Internet access
- Computers or tablets
- Note-taking materials (paper, pens, or digital tools)
- Handouts with criteria for evaluation (e.g., cost, spatial resolution, temporal resolution, invasiveness, accessibility)

#### ***Time***

45 minutes

#### ***Instructions***

##### ***Introduction (5 minutes):***

1. Introduce the activity and explain the goal: to compare fMRI, fNIRS, EEG, and MEG using a Pugh chart.
2. Briefly describe each brain imaging technique and the criteria for evaluation (cost, spatial resolution, temporal resolution, invasiveness, accessibility).

##### ***Group Formation (2 minutes):***

3. Divide the class into small buzz groups of 3-4 students.

***Research and Discussion (10 minutes):***

4. Assign each group one brain imaging technique (fMRI, fNIRS, EEG, MEG) to research and discuss.
5. Have each group gather information about their assigned technique, focusing on the evaluation criteria.

***Criteria Development (5 minutes):***

6. Come together as a class and agree on the specific criteria and their definitions for the Pugh chart.
7. Write the criteria on the whiteboard or flip chart for reference.

***Group Analysis and Pugh Chart Creation (15 minutes):***

8. Instruct each group to fill out the Pugh chart, evaluating their assigned technique against the criteria.
9. Each group should provide a rating for their technique on each criterion (e.g., 1-5 scale) and justify their ratings.

***Presentation and Compilation (5 minutes):***

10. Have each group present their findings and ratings to the class.
11. Compile the ratings into a single Pugh chart on the whiteboard or flip chart, discussing discrepancies and reaching a consensus.

***Conclusion (3 minutes):***

12. Summarize the activity and highlight the key takeaways, emphasizing the strengths and weaknesses of each brain imaging technique and the importance of such comparative analyses in neuroengineering.



## Chapter 5: Lab introduction

In this series of lab exercises, you will explore advanced neuroimaging data analysis techniques using FreeSurfer and MATLAB. These labs will provide hands-on experience with processing and analyzing fMRI data and practical guidance on using imaging tools for data analysis.

You will start using FreeSurfer to process and analyze fMRI data from the OpenfMRI dataset ds000171. This dataset examines how neural processing of emotionally provocative auditory stimuli is altered in individuals with Major Depressive Disorder (MDD) compared to never-depressed control participants. Analyzing this data will give you insights into how emotional stimuli affect neural processing in different populations.

Next, you will follow a YouTube tutorial by Mike X Cohen, which provides step-by-step guidance on analyzing MATLAB imaging data. This tutorial will help you apply MATLAB tools to real-world data analysis scenarios, enhancing your skills in neuroimaging analysis. If you have not yet installed MATLAB, instructions for downloading it are available in Chapter 1, Lab Example 1. These labs will prepare you for further neuroimaging research and data analysis exploration.



# Chapter 5: Lab Example 1



## *Overview*

For this laboratory exercise, we will utilize FreeSurfer to process and analyze fMRI data from the OpenfMRI dataset ds000171. This dataset examines how neural processing of emotionally provocative auditory stimuli is altered in depression. The study includes 19 individuals with Major Depressive Disorder (MDD) and 20 never-depressed control participants (ND) who listened to positive and negative emotional, musical, and nonmusical stimuli during fMRI scanning.

## *Dataset Description*

- **Title:** Neural Processing of Emotional Musical and Nonmusical Stimuli in Depression
- **Participants:** 19 MDD and 20 ND
- **Tasks:** Music comprehension/production
- **Scanner:** Siemens Skyra 3T

## *Objective*

This laboratory exercise aims to process, visualize, and compare the brain activity of control and MDD subjects using FreeSurfer utilizing the dataset described above. This exercise will guide you through downloading the dataset, setting up FreeSurfer, running preprocessing with FreeSurfer, and visualizing the data in Freeview (the FreeSurfer visualization interface).

## *Installation and Setup*

Now that you know about this laboratory exercise, let's get FreeSurfer installed and running. As of the time of writing this book, FreeSurfer 7.4.1 is the current version of the toolbox; we will be covering the basic installation via a Windows 11 64-bit OS, running on an LG Gram laptop with 16GB of RAM and an integrated graphics card. FreeSurfer is intended for use on a Linux platform. Installation with Windows is less straight-forward. Following the FreeSurfer installation tutorial page is recommended, but this is meant to serve

as a brief guide. First, fill out this information to obtain a license key:  
<https://surfer.nmr.mgh.harvard.edu/registration.html>.

Now, let's begin by opening Windows PowerShell as an administrator. [*Hint: you can hit winkey+x, then select Terminal (admin)*]. We may generally refer to this environment as a “terminal” from here on out. From there, type the following command:

```
ws1 --install
```

This command will install Windows Subsystem for Linux (WSL). You will see a progression bar followed by a successful install. You will likely be prompted to generate a username and password. Using PowerShell, you will notice slightly different colors within the terminal window, indicating you are in a different environment.

Download an X server to handle the graphical visualizations. You can search for x servers and follow the installation instructions or install one of the recommended options from FreeSurfer; this includes Xming and VcXsrv. The installation process here is straightforward: follow the default options and proceed.

Next, let's return to the Ubuntu terminal. If you closed out of it or are returning, re-open PowerShell and type “*wsl*” (enter), then type “*cd*” (enter). You are now in the Ubuntu environment's home directory. Finally, download FreeSurfer with the following\* (See note below):

```
wget  
https://surfer.nmr.mgh.harvard.edu/pub/dist/freesurfer/7  
.4.1/freesurfer-linux-ubuntu22_amd64-7.4.1.tar.gz
```

*\*Note: replace the link following “wget” with the latest release found here: <https://surfer.nmr.mgh.harvard.edu/fswiki/rel7downloads>. Copy the link for the relevant Linux environment you're working in. I am installing the Ubuntu 22 amd64 tar archive link.*

This will take a while to download. While you're patiently waiting for this, now would be a good time to go back and read the learning outcomes for this chapter. Can you respond to the learning outcomes aloud in your own words? If not, that's okay; you've got plenty of time to master the concepts during your engineering journey.

Welcome back! Let's ensure the file was downloaded by typing "*ls*" (*enter*). You should see the file name listed. Let's organize our work by creating a directory to unpack and install this file.

```
sudo mkdir /usr/local/
```

This folder should already exist. If you installed the tar.gz file type, now type:

```
sudo tar -xzf freesurfer-linux-ubuntu22_amd64-  
7.4.1.tar.gz -C /usr/local
```

You're almost there! Now, enter the following commands to setup environmental variables, making it easier to navigate within the terminal:

```
export FREESURFER_HOME=/usr/local/freesurfer/  
echo "export FREESURFER_HOME=/usr/local/freesurfer/">>  
~/.bashrc
```

Typing "*ls* *\$FREESURFER\_HOME*" should list several folders of the FreeSurfer install. You were told to complete the registration information and obtain a license.txt file earlier. Download it and copy it in your Linux directory using:

```
cp /mnt/c/Users/bfugg/Downloads/license.txt ~/
```

Typing "*ls*" should show the license.txt file listed. Next, enter the following:

```
echo "export FS_LICENSE=$HOME/license.txt" >> ~/.bashrc
```

Configure display settings:

```
echo "export DISPLAY=:0" >> ~/.bashrc
```

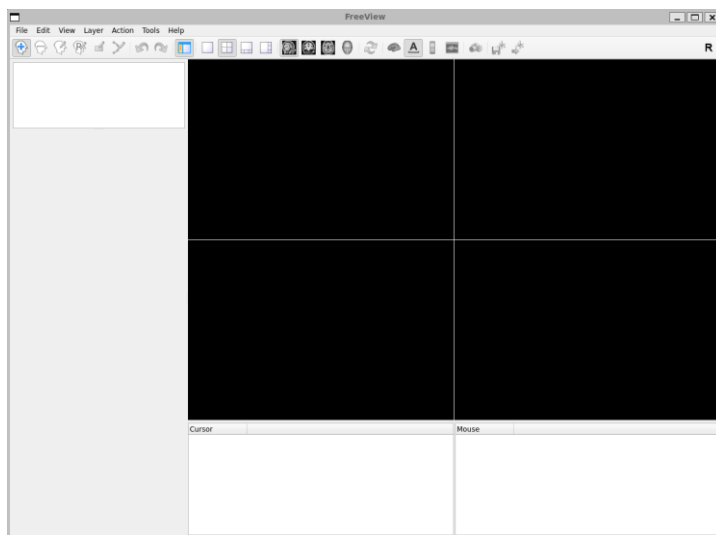


Figure 5.3: Display Settings

```
source ~/.bashrc
```

Run Xlaunch, which we installed earlier, then try to run Freeview in the terminal with:

```
freeview
```

If the window opened, as in Fig. 5.3, great job. Let's proceed to download the dataset we want to analyze. You can download or use any data that suites your experiment goals.

Visit the [OpenfMRI](https://openfmri.org/) data page and download the ds000171 accession number dataset.

<https://openfmri.org/dataset/ds000171/>

Extract the folders you downloaded into your WSL home directory:

```
mkdir -p ~/openfmri_ds000171/controls
mkdir -p ~/openfmri_ds000171/mdd
tar -xzf controls.tar.gz -C
~/openfmri_ds000171/controls
tar -xzf mdd.tar.gz -C ~/openfmri_ds000171/mdd
```

## *Preprocessing*

If you explore the data structure within the controls and MDD folders, you'll notice several subfolders separating each subject data and anatomical and functional fMRI data. Let's work with subject 01 data from the control and MDD groups. Setup a SUBJECTS\_DIR environment variable:

```
export SUBJECTS_DIR=~/openfmri_ds000171
```

Run “recon-all” for the control subject and then the MDD subject; this might take a long time to process.

```
recon-all -s control_sub-01 -i
~/openfmri_ds000171/controls/sub-control01/anat/sub-
control01_T1w.nii.gz -all
recon-all -s mdd_sub-01 -i ~/openfmri_ds000171/mdd/sub-
mdd01/anat/sub-mdd01_T1w.nii.gz -all
```

Run ‘qcache’ for both subjects to smooth the data.

```
recon-all -s control_sub-01 -qcache
recon-all -s mdd_sub-01 -qcache
```

The ‘recon-all’ command in FreeSurfer is a preprocessing tool that generates detailed 3D models of the brain's structure, essential for accurate registration and analysis of functional MRI data in subsequent steps.

Now, you must run FS-FAST (FreeSurfer Functional Analysis Stream) preprocessing. FSFAST performs essential preprocessing steps for functional data, such as motion correction, slice timing, spatial normalization, and smoothing. First, ensure your data is organized into the hierarchy FSFAST expects. This requires your data to be organized into run directories (001,002, etc) within a ‘bold’ subfolder for each subject. This can be accomplished by the following:

```
mkdir -p ~/openfmri_ds000171/analysis/control_sub-01/bold/001
mkdir -p ~/openfmri_ds000171/analysis/control_sub-01/bold/002
mkdir -p ~/openfmri_ds000171/analysis/mdd_sub-01/bold/001
mkdir -p ~/openfmri_ds000171/analysis/mdd_sub-01/bold/002
```

Now move and rename the functional data files into these directories:

```
mv ~/openfmri_ds000171/controls/sub-control01/func/sub-control01_task-music_run-1_bold.nii.gz
~/openfmri_ds000171/analysis/control_sub-01/bold/001/f.nii.gz
mv ~/openfmri_ds000171/controls/sub-control01/func/sub-control01_task-music_run-1_events.par
~/openfmri_ds000171/analysis/control_sub-01/bold/001/
mv ~/openfmri_ds000171/controls/sub-control01/func/sub-control01_task-nonmusic_run-4_bold.nii.gz
~/openfmri_ds000171/analysis/control_sub-01/bold/002/f.nii.gz
mv ~/openfmri_ds000171/controls/sub-control01/func/sub-control01_task-nonmusic_run-4_events.par
~/openfmri_ds000171/analysis/control_sub-01/bold/002/
mv ~/openfmri_ds000171/mdd/sub-mdd01/func/sub-mdd01_task-music_run-1_bold.nii.gz
~/openfmri_ds000171/analysis/mdd_sub-01/bold/001/f.nii.gz
```

```
mv ~/openfmri_ds000171/mdd/sub-mdd01/func/sub-
mdd01_task-music_run-1_events.par
~/openfmri_ds000171/analysis/mdd_sub-01/bold/001/
mv ~/openfmri_ds000171/mdd/sub-mdd01/func/sub-
mdd01_task-nonmusic_run-4_bold.nii.gz
~/openfmri_ds000171/analysis/mdd_sub-
01/bold/002/f.nii.gz
mv ~/openfmri_ds000171/mdd/sub-mdd01/func/sub-
mdd01_task-nonmusic_run-4_events.par
~/openfmri_ds000171/analysis/mdd_sub-01/bold/002/
```

To reiterate, for this example, we are only working with a few of the run files for this walk-through, but you should organize your data into this structure for all your data if you plan to conduct group-level analysis. Create a text file in each session folder containing the subject name that corresponds to the anatomical data processed by recon-all earlier:

```
echo "control_sub-01" >
~/openfmri_ds000171/analysis/control_sub-01/subjectname
echo "mdd_sub-01" >
~/openfmri_ds000171/analysis/mdd_sub-01/subjectname
```

Now we are ready to run FS-FAST preprocessing:

```
export SUBJECTS_DIR=~/openfmri_ds000171/analysis
preproc-sess -s control_sub-01 -fsd bold -stc up -
surface fsaverage lhrh -mni305 -fwhm 5 -per-run
preproc-sess -s mdd_sub-01 -fsd bold -stc up -surface
fsaverage lhrh -mni305 -fwhm 5 -per-run
```

After completing this, you can check the registration quality using the following codes. A value closer to 0 indicates good registration:

```
tkregister-sess -s mdd_sub-01 -fsd bold -per-run -bbr-
sum
```

Next, we need to analyze the data, which is called first-level analysis. For simplicity, we will only analyze one run for two subjects, one control, and one MDD subject. However, this will not yield results that can be interpreted to any degree of certainty. Realistically, you will perform the analysis on the entire data set to increase the statistical robustness of your analysis and form more reliable conclusions. Let's review the data we are working with and set up our analysis, create contrasts, and run the analysis.

Recall that the dataset we are working with analyzed Major Depressive Disorder (MDD) subjects and never-depressed control participants (ND), who listened to positive and negative emotional musical and nonmusical stimuli during fMRI scanning. The participants would listen to a tone (null-condition), then listen to either positive or negative music, then respond to the researchers if they thought the music was positive or negative. From this, we observe three non-null conditions: response, positive music, and negative music. As we proceed, we may decide to compare the brain response during music vs. baseline (tone) or positive music response vs negative music response, etc., where:

0 = tone

1 = response

2 = positive music

3 = negative music

Begin with setting up the analysis:

```
mkanalysis-sess \  
-fsd bold -stc up -surface fsaverage lh -fwhm 5 \  
-event-related -paradigm sub-control01_task-music_run-  
1_events.par -nconditions 3 \  
-spmhrf 0 -TR 3 -refeventdur 16 -nskip 4 -polyfit 2 \  
-analysis control.music.sm05.lh -force -per-run
```

This sets up our analysis for just the left hemisphere (lh); you can do this for both the right hemisphere (rh) and subcortical structures (mni305). We are just

going to do lh for this exercise. Run the same analysis setup for the mdd subject.

Next, create contrasts you are interested in examining. For example, the following would contrast positive and negative music vs. baseline, positive music vs baseline, and response vs baseline.

```
mkcontrast-sess -s control_sub-01 -analysis  
control.music.sm05.lh -contrast combined_music-vs-rest -  
a 2 -a 3  
mkcontrast-sess -s control_sub-01 -analysis  
control.music.sm05.lh -contrast pos_music-vs-rest -a 2  
mkcontrast-sess -s control_sub-01 -analysis  
control.music.sm05.lh -contrast response-vs-rest -a 1
```

Again, you can use any contrasts or nomenclature you'd like. For example, the values -a 2 -a 3 indicate you want conditions 2 and 3 active. You should create contrasts for the mdd subject as well. Finally, run the analysis with:

```
selxavg3-sess -s control_sub-01 -analysis  
control.music.sm05.lh  
selxavg3-sess -s mdd_sub-01 -analysis mdd.music.sm05.lh
```

The above commands are just for the left hemisphere; you would repeat each command for rh and mni305.

Suppose you have made it this far. Congratulations! You have completed a first-level analysis of one subject (Fig. 5.4). You can now visualize your data.

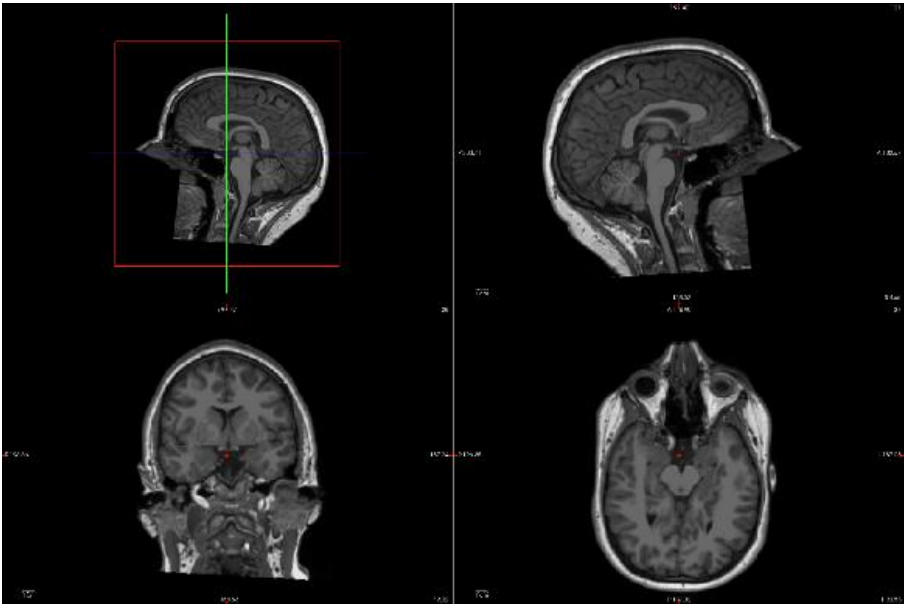


Figure 5.4: Set up for analysis

## *Visualization and Comparison*

We can start by viewing the basic anatomical data (Fig. 5.5). Open freeview with your terminal's “freeview” command. Select load volume and locate the “mri” directory of the subject you wish to look at. Alternatively, you can look

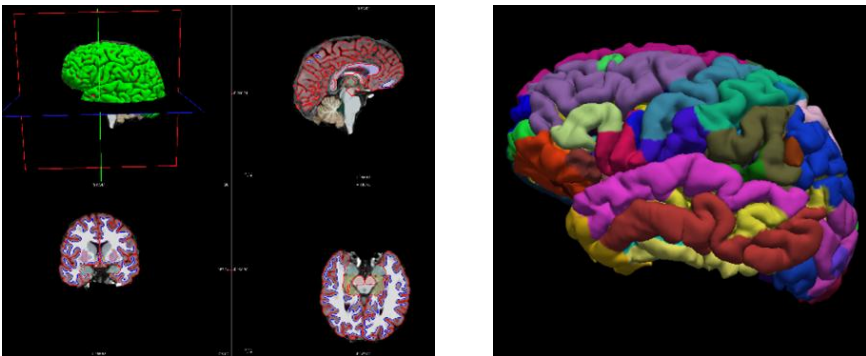


Figure 5.5: Basic Anatomical Data

at other interesting outputs from recon-all, such as the segmentations, surfaces, or masks. Below are some examples of the view you can load that may assist you in your research goals. Many of these can be generated by utilizing the Freeview GUI screen and loading the volumes or surfaces you wish to investigate. Adjusting the opacity and overlays on the left side of the GUI provides additional ways to customize the viewport.

If you followed the directions above, we analyzed three non-null conditions during the analysis.

The inflated left-hemisphere view shows combined music vs rest in control subjects to the right. The red and yellow highlights show significant activations of the superior temporal gyrus. Red indicates a statistically significant difference in activation during music vs baseline (tones).

For the major depressive disorder subject, let's look at the results for their combined music vs baseline (tone). You can see similar areas of activation in the left hemisphere. If you analyzed the right hemisphere and the subcortical structures, you could examine which internal structures become activated in each subject, as shown below.

The applications of this tool are limitless in your journey to studying fMRI. From here, you could analyze every control subject and create a statistically robust representation of brain activations during music exposure compared to

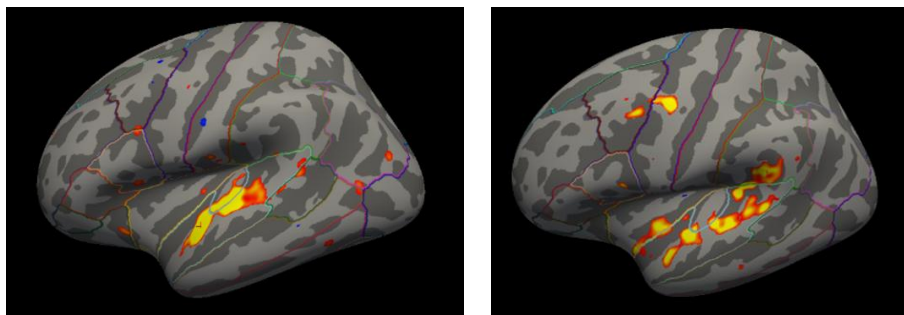


Figure 5.6: Combined music vs rest in control subjects

the resting state. Or you could proceed to compare the activations of the control subject to the depressive subjects.

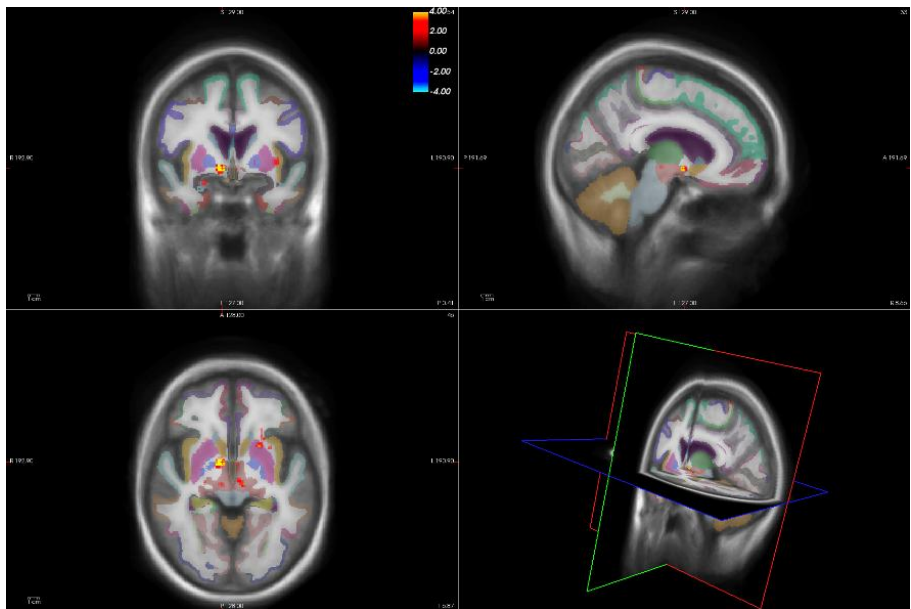


Figure 5.7: Combined music vs rest in major depressive disorder subjects



# Chapter 5: Lab Example 2



## Overview

In this lab example, you will follow a YouTube tutorial by Mike X Cohen [1]. Mike X Cohen has many tutorials on his YouTube platform, where he guides viewers through many examples of imaging data analysis using engineering tools. For this lab, we will be using MATLAB as our tool. You should already have MATLAB downloaded; if you do not, instructions on downloading MATLAB can be found in Chapter 1, Lab Example 1.

To get started, here is a link to Mike X Cohen's YouTube page:

<https://www.youtube.com/@mikexcohen1>

Once you are on his page, you want to navigate to the Playlists tab and then find the Essentials of Neuroscience with MATLAB playlist. When the playlist is open, you will notice on the right-hand side that there are several modules in this playlist. For this lab example, we will follow Module 4 (fMRI). In this module, Mike X Cohen provides an example of processing fMRI data from an experiment using visual stimuli. As mentioned in Chapter 8, the brain's visual cortex is retinotopically organized, and in this lab, we will be able to see that organization. Mike X Cohen uses a data set from Kay et al., 2020 [134]. In this study, the researchers are testing a new method called Temporal Decomposition to improve the spatial resolution of fMRI data analyzed with tasked tasks.

## Video 1

In Module 4-1, Mike X Cohen explains the task in this study. In the study, participants looked at visual stimuli, where they needed to look at the dot in the center of a ring. The ring's eccentricity changed in size throughout six conditions, where in condition one, the ring was closest to the dot, and in condition six, it was furthest away from the dot.

This task presents visual stimuli from different distances from the fovea. Due to the retinotopic organization of the visual cortex, the visual stimuli produced by condition one, where the ring is closest to the center dot, activate central

vision in the fovea. Higher visual cortex activation will occur at the calcarine fissure (refer to Chapter 8 Fig. 8.6 [135]). As the visual gets further from the center, the stimuli will progressively move away from the calcarine fissure. You will see this progression of activation in the images generated by the lab. After you have found Mike X Cohen’s page and this module, go to the caption of the Module 4-1 video. In the caption, Mike X Cohen has provided all the code and data files needed for this lab. Once you click on the link, a file will download. In this folder, you will see several MATLAB files. You will first want to open the `exampledataset.mat` file and an Import Wizard box will pop up. You will want to click finished and have the data imported into your workspace in MATLAB.

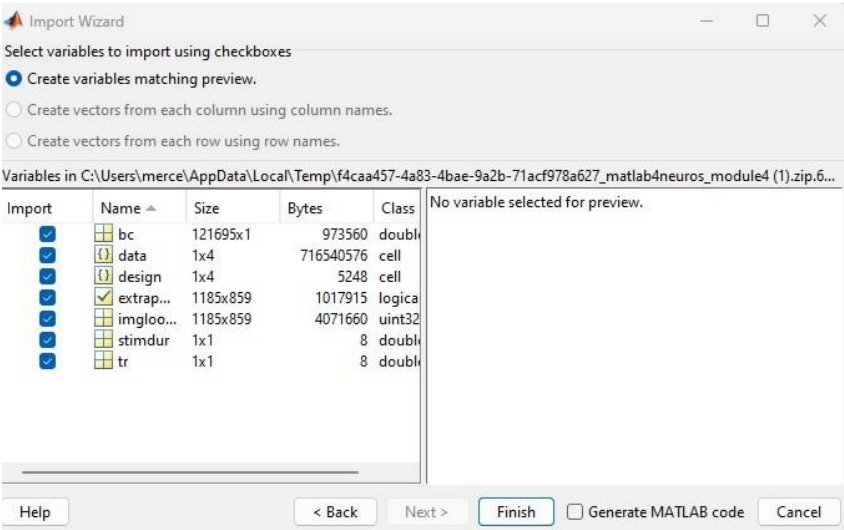


Figure 5.8: Inserting example data

Once you have finished this, you will want to navigate to `matlab4neuros_module4_partial.mat` file. This file contains the code Mike X Cohen will walk you through in each video, where you can code with him to

produce the figures. It is recommended that you use this code in a live script. When the code is uploaded into MATLAB, you will be prompted to “Open this file as a live script.” You will want to click “Open as a live script.” You will then watch Mike X Cohen’s videos for Module 4 (fMRI). This lab

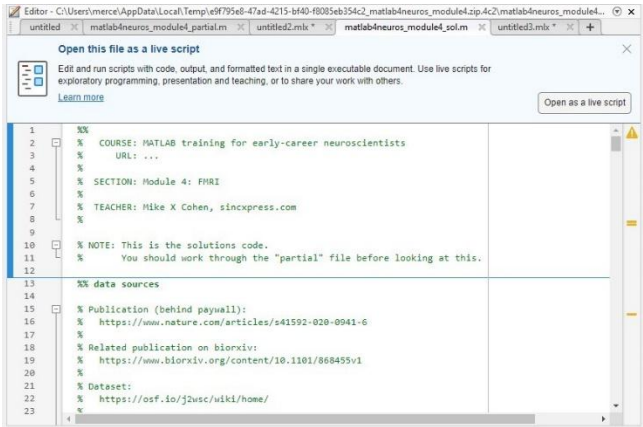


Figure 5.9: Live Script View

has several parts, during which you will create flat maps of the fMRI data, different visualizations for the BOLD response, and conduct a t-test.

## Video 2

In Video 2, you can create and visualize the flat maps. A flat map is a two-dimensional representation of the brain’s cortical surface. Flat maps are made by reconstructing the cortical surface and then inflating it to smooth the gyri and sulci. Then, the surface is flattened into a 2D map, preserving the spatial relationships of the cortical regions. Here is a video from YouTube from MNE-Python that shows how flat maps are created.

<https://www.youtube.com/watch?v=OOy7t1yq8IM>

You can see the flat maps by the end of Module 4, Video 2 of Mike X Cohen’s tutorial (Fig. 5.10).

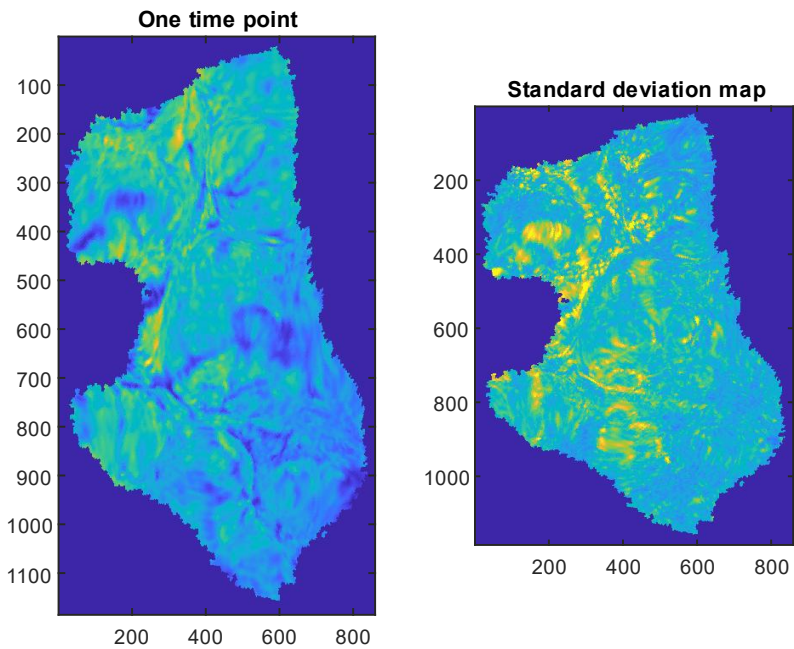


Figure 5.10: Visualizing flat maps

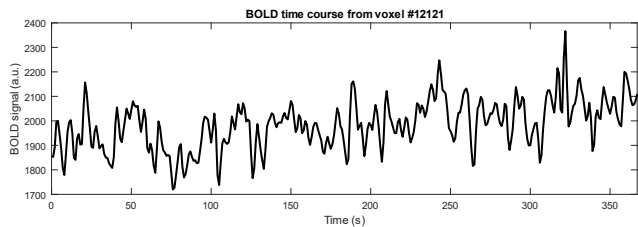


Figure 5.11: Bold Time Course

### Video 3

After you have completed Video 2, you will move on to Video 3, where you will preprocess the BOLD signal data. In this video, you will produce a figure showing the BOLD time course from a specific voxel (Fig. 5.11). In the figure,

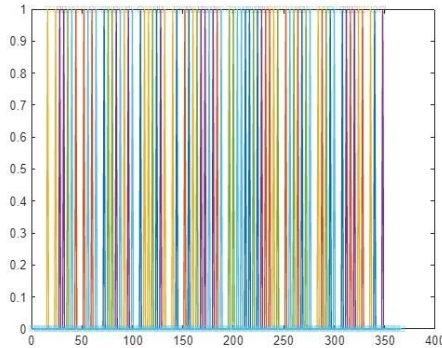


Figure 5.12: Design Matrix over time

the x-axis represents the time in seconds (s), and the y-axis represents the intensity of the BOLD signal in arbitrary units (a.u.). This figure depicts changes in the blood oxygenation of this voxel over time.

### Video 4

Once you finish with Video 3, you will move onto Video 4, exploring the design matrix the researchers used in their experimentation. In this video, you will produce three different visualizations.

The first figure you create depicts when they presented each stimulus category over time (Fig. 5.12).

Can you say that it is quite hard to understand the design matrix when it is in this form? Mike X Cohen explains this in this video and shows you how to convert this into a gray figure using the following code.

```
% perhaps it's easier to visualize as an image?
```

```
imagesc(design{1})
xlabel('Condition number')
ylabel('Time (TR)')
colormap gray
```

Your figure will now look at Fig. 5.13. Now, it is much easier to see which condition (x-axis) has been presented over time (y-axis). The next step you will take in this video is to plot the events over the time course of the BOLD response. You will produce a figure that looks like Fig. 5.14.

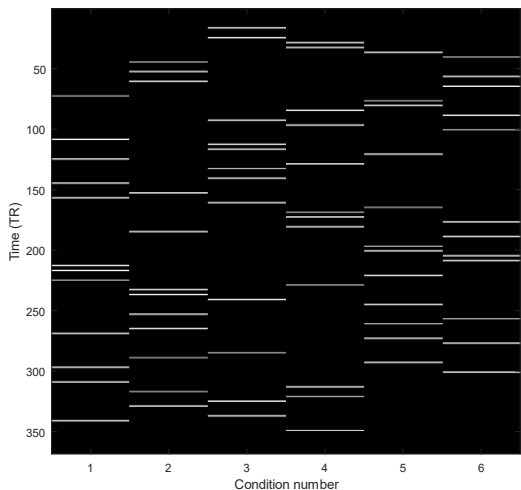


Figure 5.13: Gray Colormap of Design Matrix

Next, you will produce Fig. 5.15, visualizing the even related data matrix. It will look like this. This figure shows the differences in BOLD activity over time (x-axis) for the different voxel indices (y-axis). This matrix allows for visualizing how the BOLD signal varies across the different voxels during a task over time.

*Video 5*

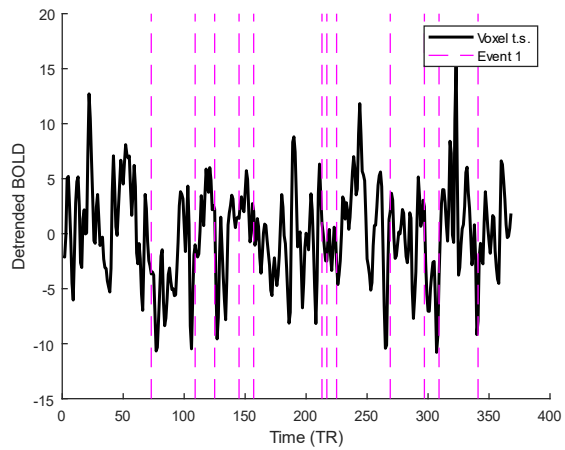


Figure 5.14: Events over time with BOLD response

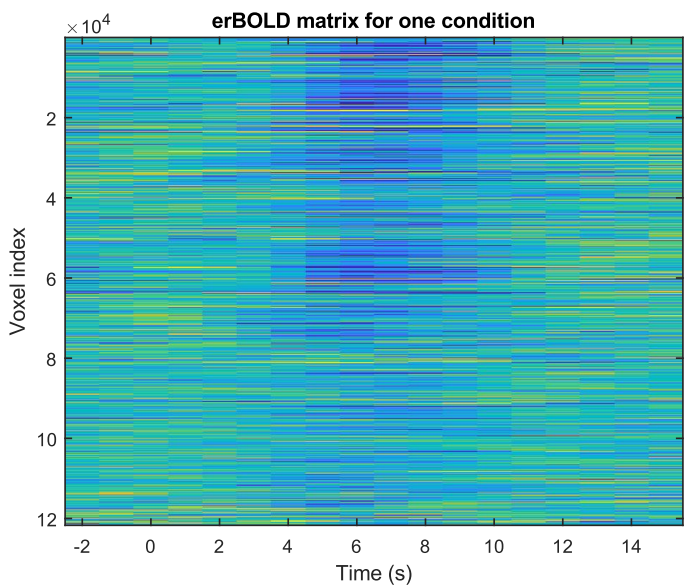


Figure 5.15: BOLD signal across voxels during task

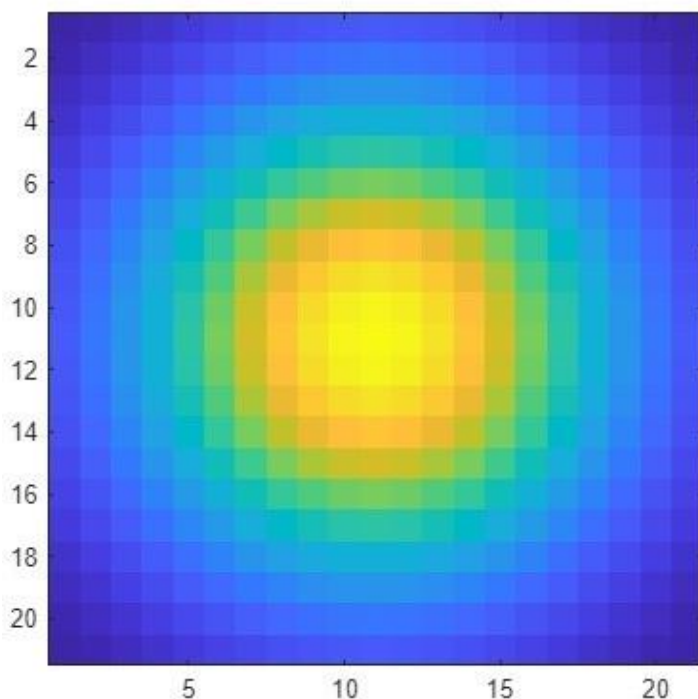


Figure 5.16: Gaussian Heat Map

Next, you will watch Module 4, Video 5 of Mike X Cohen's tutorial, where you will create an animation of the bold response over time. You will first make a 2D Gaussian distribution heat map (Fig. 5.16). In a Gaussian distribution, values are highest in the center and taper off symmetrically toward the edges.

Next, you will produce the animation, in which you will see the progression of the BOLD response over time for each condition of the visual task from the study.

## ***Video 6***

Next, you will watch Module 4, Video 6 of the tutorial, where Mike X Cohen will set you up for the statistical analysis of the data, and you will create a new

data visualization. Following this tutorial, we encountered an error message stating, “Dot indexing is not supported for variables of this type.” This error was fixed by coding in

```
datacursormode on
```

Under % step 1: turn datacursormode on and click on a map instead of put it in the command window.

Your figure will look at Fig. 5.17.

Here, you see the BOLD response (y-axis) over time (x-axis) for the different conditions for the selected voxel.

**Video 7**

In the final video, Module 4, Video 7 of the Mike X Cohen tutorial series, you will conduct a t-test and visualize it on a map. A t-test is a statistical test that compares the means of two groups to determine if they are significantly different from each other. In this case, you will compare the differences in

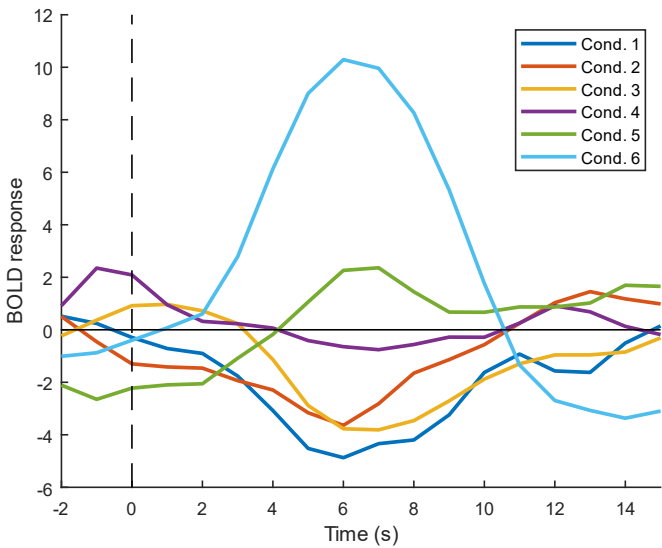


Figure 5.17: BOLD response over time

BOLD activity for condition one, where the ring is closest to the center dot, and condition six, where the ring is the furthest from the center dot. The figure you will generate looks like this.

In Fig. 5.17, you will see red and blue colors. Red represents areas where condition one has a significantly higher BOLD response than condition six. This makes sense since the red coloring is located at the calcarine fissure. Blue represents areas where condition six has significantly higher BOLD responses than condition one. This makes sense since blue is farther away from the calcarine fissure, indicating visual stimuli in peripheral vision. It is worth noting that Mike X Cohen explains why a t-test is not the best way to analyze this data. This is because there are a lot of variances in the BOLD response that will be ignored when conducting a t-test at a certain time. However,

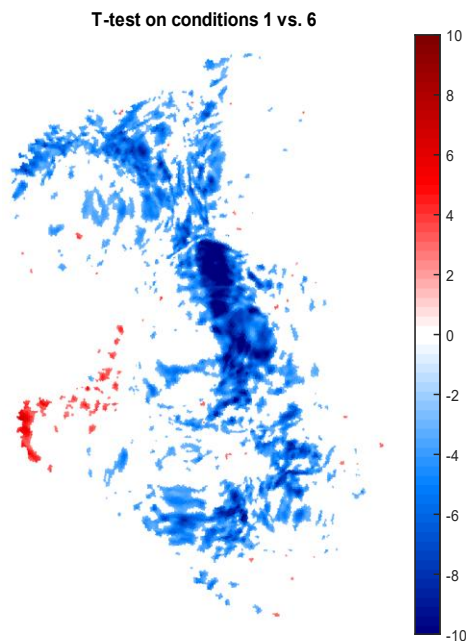


Figure 5.18: T-test map

learning how to conduct t-tests in MATLAB is good since they are fundamental statistical tests.

That will conclude the fMRI tutorial from Mike X Cohen on YouTube. Mike X Cohen provides several other examples of understanding data from imaging techniques in different tutorials on his YouTube page, which was linked at the beginning of this lab.

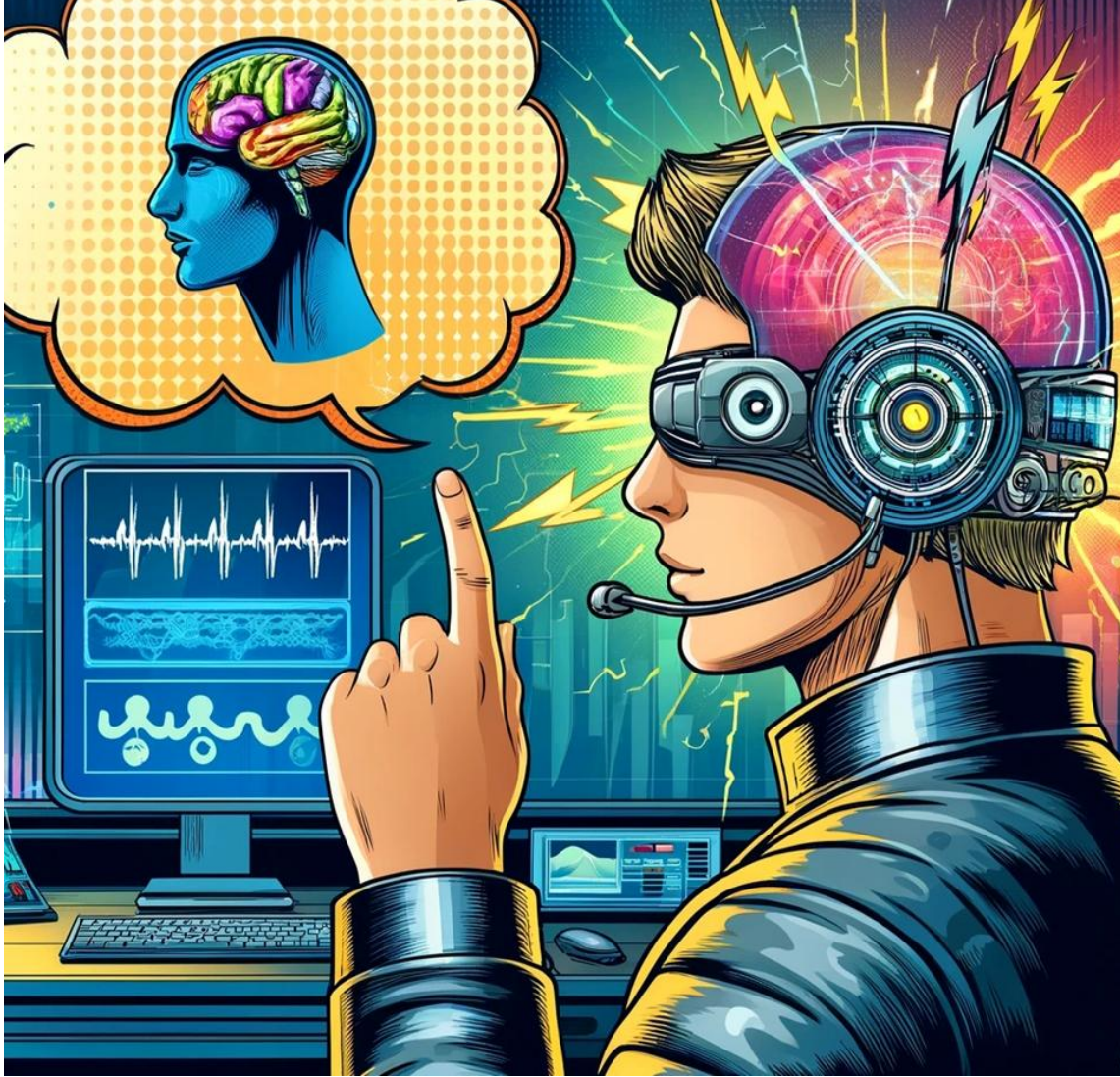
YouTube is a tool that you can use to find a lot of tutorials using engineering tools to get started learning the platforms.

## Acknowledgments

We sincerely thank Mike X Cohen for his invaluable contributions to our project. Special thanks go to Mike for allowing us to use his comprehensive YouTube tutorial as a reference for our lab example. His clear explanations and expert insights have greatly enhanced our understanding and implementation of the techniques discussed. We highly recommend exploring his channel for anyone interested in diving deeper into this field.







## Chapter 6

# Bridging Minds and Machines: Brain-Computer Interfaces

# Introduction and Learning Objectives

So far in this textbook, you have learned about the fundamental building blocks of the brain and different ways that researchers use to try and understand the brain, whether that be computational, such as in Chapters 2 and 3, or through engineering tools, such as those discussed in Chapters 4 and 5. In this next chapter, we will explore Brain-Computer Interfaces (BCIs) and how researchers leverage our understanding of the brain to develop technologies that enable direct communication between the mind and machines. We will discuss the history of BCIs, their work, ethical considerations, and future implications of these technologies. By the end of this chapter, you will be able to:

1. *Identify and explain the critical hardware and software components involved in BCIs, including capturing brain signals, signal processing, and output devices.*
2. *Discuss the advantages and disadvantages of comparing invasive and noninvasive BCIs.*
3. *Grasp the ethical considerations and potential societal impacts of BCI technologies.*

## Introduction to Brain-Computer Interfaces (BCIs)

### *Definition of BCIs*

Brain-computer interfaces (BCIs) allow communication between the brain and external devices, offering individuals new ways to interact with their environment. By capturing and interpreting brain signals, BCIs can empower individuals to control computers or operate prosthetic limbs using only their thoughts. This technology can significantly improve the quality of life for those facing severe physical disabilities, helping them regain lost functions. BCIs achieve this by creating an interface that can translate neural activity into commands. This process begins with detecting brain signals through various methods such as EEG or MEG (Chapter 4), fMRI (Chapter 5), or invasive

approaches involving implanted electrodes, which we will discuss in more detail later in this chapter. The detected signals are amplified and processed to filter noise and extract features. Advanced algorithms decode these features and translate them into commands to control external devices, whether computers or prosthetics [136].

The applications of BCIs can be vast. In the medical field, BCIs can be used to restore communication and mobility for patients who suffer from disabilities caused by disease, injury, or stroke. For example, a person who suffers a spinal cord injury and has lost the ability to move their limbs can use BCIs to operate motorized wheelchairs or robotic prosthetics to regain levels of independence [137]. Beyond medical applications, BCIs are also being researched to enhance human-computer interaction, such as gaming and virtual reality experiences (Chapter 10). The creation and advancement of BCIs have opened a new frontier in how we interact with technology.

***Brief history and evolution of BCIs***

Dr. Grey Walter was one of the earliest researchers to develop BCIs (Fig. 6.1 [138]). In the 1960s, he demonstrated the potential for using brain signals to control external devices [139]. His work laid a foundation for the future of direct mind-to-machine communication. In the 1970s, Dr. Eberhard Fetz made significant

contributions to the field by showing that monkeys can be trained to control the firing rates of neurons in the motor cortex. He proved that neural activity can be harnessed to control external devices [140].



Figure 6.1: Dr. Grey Walter and Vivian Dovey 1943 [138]

These pioneers in the field of BCIs set the stage for the creation of more sophisticated BCI systems.

BCIs gained momentum in the 1990s with the advancement of computer technology and neuroimaging techniques fueling this growth. These advancements allowed for a more precise and detailed interpretation of neural activity. Researchers commonly used EEGs to capture brain signals in these early stages of BCI development, and these early noninvasive BCIs were crucial in demonstrating the feasibility of brain-controlled communication and control. In 1998, there was a significant breakthrough in BCI development when Dr. Phillip Kennedy implanted the first intracortical BCI in a patient. This invasive BCI allowed a paralyzed individual to control a computer cursor by recording motor cortex activity [141]. This milestone showed the potential for invasive BCIs for individuals with severe motor impairments.

In the early 2000s, this field experienced significant growth due to improvements in signal processing algorithms and machine learning techniques. These systems could not accurately decode the brain signals and were more applicable to real-world applications. During this time, researchers focused on extending these technologies outside the lab into a clinical setting to improve the quality of life of those with disabilities. The 2010s brought big companies such as Neuralink and BrainGate into the BCI field, where these companies wanted to develop more precise and varied controlled BCIs. Founded by Elon Musk, Neuralink aims to create BCIs that seamlessly integrate with the human brain, with the potential of a wide range of applications from medical rehabilitation and cognitive enhancement. BrainGate has shown significant progress in developing BCIs that allow individuals with tetraplegia paralysis due to injury of the cervical spinal cord, where individuals experience motor loss of all four limbs, to control robotic limbs and computer interfaces [137].

The history and milestones of BCIs relate to a rapidly advancing field that is increasingly integrating into medical care and daily life. As researchers continue to push the boundaries in this field, BCIs hold promise in transforming the lives of individuals with disabilities, enhancing human capabilities, and enhancing our interaction with technology.

# Components of BCIs

Now that we have discussed the foundations of BCIs and a general idea of their function, we will discuss how BCIs can bridge mind and machine in deeper detail.

## Capturing Brain Signals (EEG, fMRI)

Previously in this book, you explored techniques that capture electrical (Chapter 4 EEG/MEG) and hemodynamic signals (Chapter 5 fMRI and fNIR). These signals can also be captured for capturing brain signals for BCIs. For a quick recall, EEGs record electrical activity along the scalp by dating voltage fluctuations resulting from ionic current flows within the neurons. fMRIs measure brain activity based on blood flow; when a brain area is in use, we expect an increase in blood flow, allowing researchers to understand brain active regions. We will focus on how these techniques are used in BCIs.

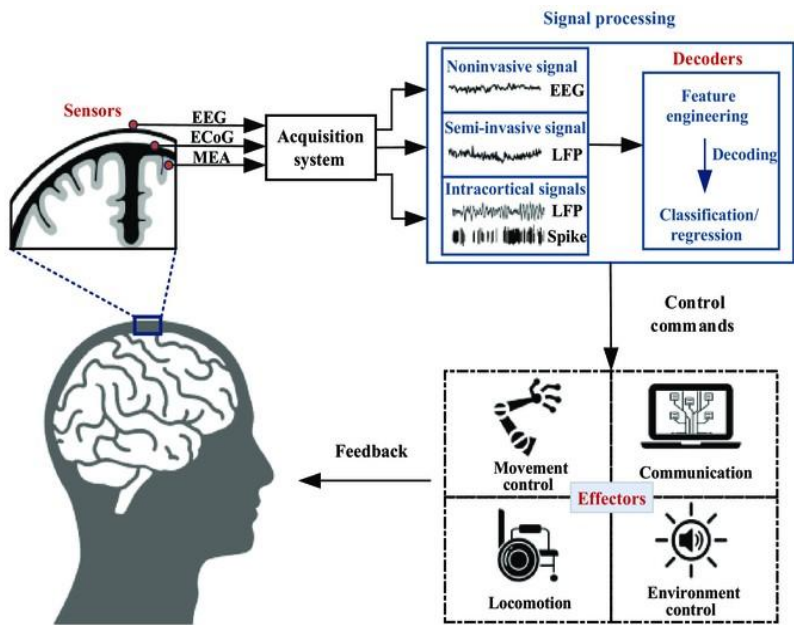


Figure 6.2: EEG based BCI for capturing electrical activity [145]

## ***EEG/MEG***

EEG is used in BCIs since it offers several advantages, such as being non-invasive, having high temporal resolution, and relatively low costs. In a BCI system, the EEG electrodes capture the brain's electrical activity, which amplifies those signals. Features such as event-related potentials (ERPs) and sensorimotor rhythms (SMRs) are extracted from the EEG signals to interpret the users' intentions into a command. For example, a P300-based BCI Speller used EEG to allow users to select letters on a screen by focusing on a character. These BCIs have been used to enable patients with motor speech impairments, such as those with amyotrophic lateral sclerosis (ALS), which will be discussed more in Chapter 12, to be able to communicate more efficiently [142], [143], [144]. The hardware used for EEG-based BCIs includes the electrode caps, amplifiers, and data acquisition units, as discussed in Chapter 4. Fig. 6.2 [145] shows an EEG-based BCI system.

## ***fMRI/fNIRs***

fMRI can also be used in BCIs due to its high spatial resolution and ability to orient BCIs to specific brain areas associated with tasks or thoughts. Although fMRIs disadvantages of being expensive and size make it impractical for BCIs for daily life activities, they can provide insights into the brain architectures and identify patterns associated with mental states and intentions. These insights, such as understanding brain areas related to imagining specific movements or objects, can help translate these signs into control commands for external devices [146]. The hardware used in fMRI-based BCIs includes the fMRI scanners, as discussed in Chapter 4. While EEG can offer real-time measurements with high temporal resolution, they lack the spatial precision of fMRI. On the other hand, fMRI can provide detailed spatial maps of brain activity but is limited by its temporal resolution and high costs. Leveraging both technologies can have the potential to provide a more comprehensive approach to BCI research and development since it can provide both precise temporal and spatial information about brain activity [147].

Capturing brain activity is only the first step in a successful BCI. Next, we will discuss what happens after this data capture and how these measurements of brain activity are processed to produce control commands to external devices.

## ***Signal Processing and Feature Extraction***

Signal processing is crucial in translating raw brain signals into actionable commands controlling external devices. This process involves multiple steps, each critical for ensuring that the BCI system is reliable and accurate, allowing users to interact with the world in novel ways, especially in assistive technologies for individuals with disabilities.

The first step in signal processing for BCIs is reducing noise from the raw signals. Brain signals, particularly those captured by EEGs or fMRI, are inherently noisy due to various factors, including physiological artifacts and environmental interferences. There are different ways to reduce noise. Independent Component Analysis (ICA) is a statistical technique that separates a multivariate signal into additive, independent components. It is particularly useful in isolating and removing artifacts, such as eye blinks, from EEG data without losing critical neural information. Common Average Referencing (CAR) is a spatial filtering technique where the average of the signals from all electrodes is subtracted from each electrode's signal. This method helps reduce common noise across the electrodes, enhancing the signal-to-noise ratio. Lastly, Adaptive filtering dynamically adjusts the filtering process based on the properties of the incoming signals. It effectively reduces noise that changes over time, such as slow drifts in EEG signals caused by sweat or electrode movement. These noise reduction techniques are essential because any residual noise can significantly impact the accuracy of the BCI, leading to incorrect interpretations of the user's intentions [148].

After noise reduction, features from the signal must be extracted to identify key brain signal characteristics corresponding to the users' intentions. Time-domain, frequency domain, and time-frequency analyses are commonly used in feature extraction for BCIs.

### ***Time Domain Analysis***

Time-domain features such as amplitude, mean, and variance are extracted directly from the signal waveform. These features are often used in real-time BCIs because they are straightforward to compute and provide immediate insights into brain activity.

### ***Frequency Domain Analysis***

Frequency-domain analysis involves transforming the time-domain signal into the frequency domain using techniques like the Fast Fourier Transform (FFT). This approach helps identify rhythmic activity, such as alpha, beta, and gamma waves, corresponding to different mental states or cognitive processes.

### ***Time-Frequency Analysis***

Time-frequency analysis combines the benefits of both time and frequency domain analyses. Techniques like the Short-Time Fourier Transform (STFT) or wavelet transform are used to analyze how the frequency content of a signal evolves. This is particularly useful for detecting transient events, such as motor imagery, where the brain's activity changes quickly.

These features are then used to train machine learning algorithms (Chapter 3) to understand user intentions [149]. Supervises learning algorithms such as Support Vector Machines (SVM), Linear Discriminant Analysis (LDA), and Convolutional Neural Networks (CNN), which can be trained to label datasets to classify brain signals.

#### ***Support Vector Machines (SVM):***

SVM is a popular machine learning algorithm that finds the optimal boundary (or hyperplane) separating different brain signal classes. It is particularly effective for binary classification tasks, such as distinguishing between "left" and "right" motor imagery.

#### ***Linear Discriminant Analysis (LDA):***

LDA is a simple yet powerful classifier that assumes linear separability between classes. It works well when the brain signals exhibit a Gaussian distribution and is computationally efficient, making it suitable for real-time BCI applications.

#### ***Convolutional Neural Networks (CNNs)***

CNNs, a type of deep learning algorithm, have shown significant promise in improving the accuracy of BCIs. CNNs are particularly effective at automatically learning complex patterns in high-dimensional data, such as EEG signals, without requiring extensive manual feature extraction.

Unsupervised learning methods can include clustering and Principal Component Analysis (PCA) to identify data patterns without predefined labels.

### ***Clustering***

Unsupervised clustering algorithms group brain signal data into clusters based on their inherent similarities without needing predefined labels. This approach can be useful for exploring unknown patterns in the data or identifying distinct mental states that were not initially considered.

### ***Principal Component Analysis (PCA)***

PCA is a dimensionality reduction technique that transforms the original features into a smaller set of uncorrelated components. This reduces the complexity of the data while retaining the most important information, making it easier for the BCI system to classify signals accurately.

These algorithms often translate brain activity patterns into control commands [150]. Once brain activity is captured and interpreted, it can create commands for external devices. The machine learning models trained using these techniques are crucial for the BCI's ability to decode the user's intentions accurately. As BCI technology advances, deep learning models like CNNs are increasingly being used because of their ability to improve classification accuracy and handle the complex, non-linear nature of brain signals.

## ***Output Devices***

Various output devices can be used in BCIs, including computer cursors, robotic limbs, wheelchairs, and communication aids. These devices translate the brain signal into actions, enabling users to interact with their environment more independently. These devices include both hardware and software components.

### ***Hardware***

Hardware for output devices includes motors, sensors, and actuators that execute the appropriate commands [151].

#### **Motors**

Motors are fundamental in BCI systems where physical movement is the desired output. These motors convert the electrical commands generated by the

BCI into mechanical movement. The choice of motor is crucial because it directly affects the system's precision, speed, and responsiveness. High-precision motors, such as servo and stepper motors, are commonly used in applications where fine control is essential. For example, in a robotic limb controlled by a BCI, servo motors allow for precise control of joint angles, enabling the user to perform delicate tasks like picking up small objects or manipulating tools. In applications requiring significant force, such as controlling a BCI-powered exoskeleton, motors must provide adequate torque to support and move the user's body weight. Brushless DC motors are often used in these scenarios due to their high efficiency, power density, and smooth operation. The speed of the motor's response to BCI commands is another critical factor. Motors in BCI systems must quickly translate user intentions into movement to create a natural and intuitive interaction. This is particularly important in dynamic environments, such as BCI-controlled wheelchairs, where rapid adjustments may be needed to avoid obstacles.

## Sensors

Sensors play a vital role in providing feedback to the BCI system and ensuring accurate and safe operation of the output device. They monitor various aspects of the device's performance and the environment, allowing for real-time adjustments. Sensors that measure joints' position, angle, and velocity are crucial in robotic limbs and exoskeletons. These sensors provide feedback to the BCI system about the limb's current state, enabling precise control over movements and ensuring that the limb moves as intended by the user. These sensors measure the force or pressure the output device applies. In a prosthetic hand, for instance, force sensors can ensure that the hand grips objects with appropriate strength, preventing damage to delicate items or injury to the user.

Environmental sensors are essential for safe navigation for devices like BCI-controlled wheelchairs. Ultrasonic sensors, infrared sensors, and light detection and ranging (LIDAR) can detect obstacles and measure distances, allowing the wheelchair to avoid collisions and navigate through complex environments safely. These sensors work with the BCI to adjust the real-time movement path based on environmental conditions. In advanced prosthetics and robotic limbs, tactile sensors give the user feedback about objects' texture, shape,

and firmness. Haptic feedback mechanisms can simulate the sensation of touch, allowing users to "feel" what they are interacting with, even through a robotic device. This sensory feedback is critical for creating a more natural and effective BCI experience.

### Actuators

Actuators are devices that convert electrical signals into mechanical movement. In BCI systems, actuators are responsible for executing the commands generated by the BCI and are central to the system's ability to perform tasks in the physical world. Linear actuators produce motion in a straight line instead of rotational motion. They are commonly used in applications like adjustable beds, robotic arms, and exoskeletons, requiring controlled, linear movement. Rotary actuators produce rotational motion and are essential in devices like BCI-controlled robotic arms and prosthetic limbs. These actuators enable joints to rotate smoothly and accurately, mimicking the natural movement of human limbs. Hydraulic or pneumatic actuators might be used in applications requiring powerful and precise movements, such as in heavy-duty exoskeletons or robotic systems. These actuators provide high force and can support significant loads, making them suitable for tasks requiring strength and precision. Microactuators are used in smaller, more delicate BCI applications, such as fine-tuned robotic hands or micro-manipulation devices. These tiny actuators allow precise control at small scales, enabling tasks requiring fine motor skills.

The successful operation of a BCI system depends on the seamless integration of motors, sensors, and actuators. Each component must harmonize to translate the user's intentions into accurate, real-world actions. Advanced control systems, often incorporating feedback loops, are required to manage the interaction between the BCI, motors, sensors, and actuators. Based on sensor feedback, these systems adjust the output in real-time, ensuring smooth and accurate operation. In applications where safety is critical, such as BCI-controlled wheelchairs or exoskeletons, redundant sensors and actuators might be employed to ensure reliable operation. If one component fails, the system can switch to a backup, preventing accidents or loss of control. Many BCI systems allow customization of the hardware components to better suit the individual

user's needs. For instance, the sensors' sensitivity, the actuators' speed, and the motors' power can be adjusted to match the user's strength, dexterity, and specific requirements.

The hardware components of BCI output devices, including motors, sensors, and actuators, are essential for translating brain signals into meaningful physical actions. These components must be carefully selected and integrated to ensure the BCI system is responsive, precise, and safe. As BCI technology advances, hardware improvements will enable even more sophisticated and intuitive control of external devices, expanding the possibilities for human-computer interaction and assistive technologies.

### ***Software***

Software used in BCIs is an essential component that bridges the gap between the user's brain signals and the external devices they aim to control. The software must be highly responsive and adaptable to the unique needs of each user to facilitate a seamless and intuitive interaction with the BCI system. This adaptability is crucial for the software to accurately interpret and translate brain signals into actionable commands, ensuring the user can effectively operate the BCI-controlled devices (Fig. 6.3 [152]). BCI software is responsible for the real-time processing of brain signals, such as those captured by EEG or other neuroimaging techniques. The software applies algorithms to filter, clean, and analyze these signals to extract relevant features corresponding to the user's intended commands. Once the brain signals are processed, the software uses machine learning and pattern recognition algorithms to classify the signals into specific commands. This step is critical for translating the user's mental intentions into precise control actions for the output device.

These software systems can include graphical user interfaces (GUIs) that can provide visual feedback to the user [153]. This feedback is crucial as it allows users to see the effects of their brain signals in real-time, helping them adjust their mental strategies to improve control. For instance, in a BCI used for communication, a GUI might display a virtual keyboard where the user can select letters or words using their brain activity. GUIs in BCI software are often customizable to accommodate different user needs and preferences. Users can

modify the display layout, color schemes, and feedback mechanisms to create a comfortable and effective interface.

Additionally, BCI software usually contains features that allow users to calibrate and train the system. Calibration is a vital feature of BCI software, where the system learns to recognize the specific brain signal patterns of the user. During calibration, the user is guided through a series of tasks or exercises, and the software adjusts its algorithms to detect better and interpret the user's unique neural signatures. This step is crucial for improving the accuracy and reliability of the BCI system. Training is an ongoing process where users practice generating the specific brain signals required to control the BCI. The software often includes tools and exercises to help users improve their ability to produce clear and consistent brain signals. Over time, this training can enhance the user's proficiency in BCI, leading to more effective and seamless device control [142]. BCI software also often incorporates adaptive algorithms that continuously learn and refine their understanding of the user's brain signals. These algorithms can adjust in real-time based on the user's performance, making the system more responsive to changes in brain activity over time. This adaptability is especially important for users whose neural patterns may fluctuate due to fatigue, emotional state, or learning effects. The software can also make user-specific adjustments, such as adapting to the user's pace of interaction or the difficulty level of tasks. This ensures that the BCI remains user-friendly and effective, even as the user's needs evolve.

Software platforms used in BCIs include the BCI2000 platform, which offers suites of tools for developing BCI supplication. BCI2000 is a widely used platform in the BCI community, offering a comprehensive set of tools for developing BCI applications. It supports various signal acquisition methods, including EEG, ECoG, and others, and provides signal processing, feature extraction, and classification modules. The versatile platform supports various BCI paradigms, including motor imagery, P300-based communication, and SSVEP (Steady-State Visually Evoked Potential) systems. This versatility makes BCI2000 a popular choice for both research and clinical applications. BCI2000 has a strong community of users and developers contributing to its

ongoing development, making it a robust and well-supported platform for BCI research. Another platform is OpenViBE, an open-source system that supports real-time processing for various BCIs [154], [155]. OpenViBE is an open-source platform designed to develop and test real-time BCI systems. Being open source, it allows developers to modify and extend the platform according to their specific needs, providing a high degree of flexibility. OpenViBE supports real-time signal processing, which is crucial for applications that require immediate feedback and interaction, such as neurofeedback or real-time control of assistive devices. The platform includes powerful data visualization and feedback tools, enabling users to monitor real-time brain signals and system performance. This is particularly useful in research settings and practical BCI applications, where understanding and quickly interpreting the data is essential.

# Types of BCIs

## *Invasive vs Noninvasive*

Early in this chapter, it was mentioned that BCIs can be non-invasive or invasive (Fig. 6.4 [156]). This next section will discuss these different types of BCIs, their hardware components, typical software, and their advantages and disadvantages.

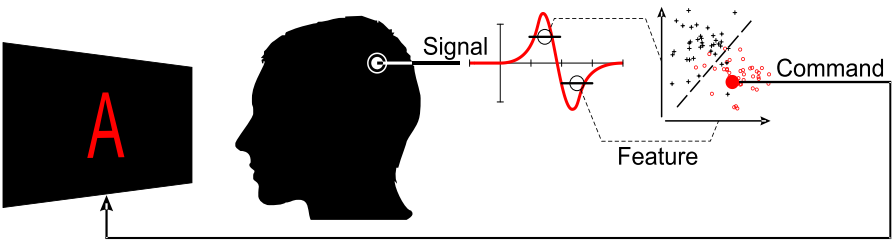


Figure 6.3: Flow of information from brain activity to external devices for BCIs, from brain activity to commands [152]

### ***Invasive BCIs***

Invasive BCIs require surgery to implant electrodes directly into brain tissue. This type of BCI is designed to capture high-resolution neural signals from specific brain regions, resulting in detailed and accurate data. The hardware components for invasive BCIs include microelectrode arrays, implantable sensors, and wireless transmission units. The materials used for these invasive BCIs must be biocompatible to mimic any adverse effects after implantation [157]. BCI systems can use electrocorticography (ECoG) grids placed on the brain's surface to capture electrical activity for motor commands for prosthetic devices or stereo electroencephalography (SEEG) that involves inserting electrodes into specific regions of deep brain structures [155]. Other systems can use intracortical implants, such as the invasive BCI in the BrainGate system. This BCI system uses an array of microelectrodes implanted in the motor cortex to control robotic limbs or computer cursors for those with paralysis [137]. Invasive BCIs offer a high spatial and temporal resolution. However, they come with significant risks. These risks can include infection, inflammation, and long-term stability issues. Additionally, surgical implantation of a BCI can pose ethical and medical challenges [158].

### ***Noninvasive BCIs***

Noninvasive BCIs do not require surgical procedures and require external devices such as EEG, which is the most used, or MEG. Noninvasive BCIs use the hardware associated with these techniques that were discussed previously. These types of BCIs are widely used for communication aids and gaming [142].

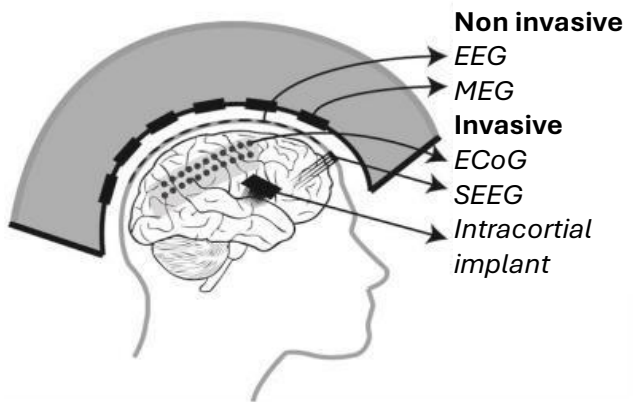


Figure 6.4: Non-invasive vs. Invasive BCI systems [156]

With no need for surgery, noninvasive BCIs are much more accessible and safer. However, they have lower signal quality and resolution and have more challenges with signal processing due to more noise [159].

## **Ethical Considerations and Future Implications**

Now that we have explored the fundamentals of BCIs, it is important to consider ethical considerations surrounding this technology and how this type of technology can impact society.

### ***Privacy and Security***

Ethical concerns of BCI systems include data privacy issues. Since BCIs capture susceptible neural activity data, serious privacy concerns exist. This data type may reveal intimate details about a person, such as their thoughts, emotions, and intentions. Additionally, issues can surround who owns this data and how to use or share it. It is essential that BCI system data is protected from unauthorized access and that there are strict privacy policies and regulations to safeguard users' information [160]. Another concern surrounding the BCI system is security and preventing hacking by unauthorized personnel. Since BCIs have the potential to influence physical actions directly, a security breach of the system can have severe consequences.

Additionally, the potential ability to manipulate thoughts or emotions through BCIs can challenge the notion of free will and personal identity. Other security concerns include mind control and surveillance. There must be extensive security measures such as encryption, secure data protocols, and robust authentication methods to protect the system from cyber threats [161],[162].

### ***Accessibility and Medical Ethics***

BCI technology has enormous potential to enhance the quality of life for individuals with disabilities. However, the accessibility of these technologies is limited due to their high cost and complexity. Additionally, hardware and software systems used in BCIs contribute to their accessibility. To bridge the gap between cutting-edge technology and its use in daily life, BCIs require

hardware and software systems that are easy to use and focused on user-centered design. Developing affordable hardware, user-friendly interfaces, and training programs are all additional efforts that are being made to reduce the cost of and simplify BCI systems to make them more accessible. Even when accessible, medical use of BCIs raises ethical concerns such as informed consent. Additionally, the potential for unintended consequences due to the risk of surgical implantation also raises concerns. Ethical review and oversight are required to ensure that these technologies are used responsibly, and that patient well-being is prioritized [163], [164].

### ***Potential Societal Impact***

The widespread adoption of BCIs can have immense effects on society. Since BCIs have the potential to enhance human capabilities, their use can lead to debates about what it means to be human. Additionally, due to accessibility concerns, BCIs can lead to new forms of inequality where those with access may gain significant advantages over those without access [160]. On the other hand, BCI technology can open new avenues of communication, learning, and interaction. Additionally, they shift cultural and social norms, leading to new forms of social interaction and collaboration. Proactive planning and inclusivity can help ensure we can maximize the benefits of BCI technology and minimize potential negative consequences [165].

## **Future Directions and Challenges**

As we conclude this chapter, it is important to assess the future directions and challenges associated with the advancement of BCI technology. This field is rapidly evolving with several trends that can change how we interact with technology. One significant modern trend is the integration of BCIs with virtual or augmented reality, which can enhance immersive experiences for gaming and rehabilitation [166]. Additionally, noninvasive BCIs are being used outside clinical settings, which makes them more accessible to more users. Another modern trend is their use in mental health applications, such as detecting and modulating emotional states. This could pave new ways for treating mental health conditions such as depression and anxiety [150].

Miniaturization of hardware, such as microelectrode arrays and flexible electronics and software innovations, is also needed for the future development of BCIs to make them more seamless and accessible. Despite these advancements, there are challenges in scaling the widespread adoption of BCIs. This challenge can arise due to the high cost of BCIs. Additionally, there are challenges in ensuring they are reliable in diverse settings where signal quality can be affected [143], [163].

## Chapter 6: Summary

In this chapter, we explored the world of BCIs, discussing their components, technologies, and ethical considerations. We assess how brain signals are captured and decoded and then used to produce commands. Through this journey of understanding this technology, you have gained a comprehensive view of how BCIs are used and how they can influence the future of human-computer interaction. As you look forward to your neural engineering journey, considering the potential and ethical impacts of BCIs is essential to ensure that we are equitable and responsible in the technologies you might create so that their full potential can be reached to benefit society.

In the next chapter, you will transition into the exciting field of neurostimulation, which explores how electrical stimulation of the brain can treat various neurological conditions and enhance cognitive functioning. You will explore two neurostimulation techniques: Deep Brain Stimulation (DBS) and Transcranial Magnetic Stimulation (TMS). These technologies can offer complementary approaches to BCIs, further expanding your knowledge of understanding and interaction with the brain.



# Chapter 6: Learning Activities

## Learning Activity 6.1

### *Basic Architecture of a BCI System*

#### *Objective*

Understand and design the basic architecture of a Brain-Computer Interface (BCI) system by creating a functional block diagram (FBD), comparing it with a reference diagram, and identifying differences, similarities, and potential improvements.



#### *Materials Needed*

- Computers or tablets with presentation software (e.g., PowerPoint)
- Internet access to view the reference diagram
- Access to the article: [Brain-Computer Interface \(BCI\) System Functional Block Diagram](#)

#### *Step-by-Step Instructions*

1. **Form Groups:**
  - Divide the class into pairs (groups of 2) to encourage collaboration.
2. **Introduction:**
  - Briefly introduce the concept of Brain-Computer Interfaces (BCIs) and their applications.
  - Explain the importance of understanding the architecture of BCI systems.
3. **Activity Part 1 - Create a Functional Block Diagram:**
  - Each group will create a PowerPoint presentation with a functional block diagram (FBD) of a BCI system.
  - The FBD should include the following basic components:
    - Signal Acquisition
    - Signal Processing (including feature extraction and classification)

- Translation Algorithm
  - Control Interface (to external devices)
  - Encourage students to think about how data flows through the system, from brain signal acquisition to the control of external devices.
4. **Activity Part 2 - Present and Share:**
- After creating their FBDs, each group will present their diagrams to the class.
  - Discuss the different approaches taken by each group.
  - **Activity Part 3 - Compare with Reference Diagram:**
    - Display Figure 2 from the article: [General Functional Block Diagram of a Brain-Computer Interface](#).
    - Give students time to study the reference diagram.
  - **Activity Part 4 - Analyze and Reflect:**
    - Students will compare their FBDs with the reference diagram in their groups.
    - Answer the following questions:
      - **What is missing?** Identify any key components or connections in the reference diagram that are absent in their diagrams.
      - **How is it different?** Note any structural or conceptual differences between their FBDs and the reference diagram.
      - **How is it similar?** Highlight the similarities in components and data flow between their FBDs and the reference diagram.
      - **How would you change it?** Based on the comparison, discuss potential improvements to their diagrams.
  - **Group Discussion:**
    - Come together as a class and discuss the findings from each group.
    - Encourage students to share insights and reflections on their observed differences and similarities.
    - Discuss the importance of each component and the overall system integration in BCI design.

- **Conclusion:**
  - Summarize the key takeaways from the activity.
  - Emphasize the importance of a well-designed architecture in the functionality and efficiency of BCI systems.
- **Follow-Up Assignment:**
  - Each student writes a short reflection (1-2 pages) on what they learned about BCI systems from this activity, including any challenges faced during the diagram creation and comparison process.

This activity will enhance students' understanding of the basic architecture of BCI systems and develop their skills in collaborative work, critical thinking, and technical communication.

## Learning Activity 6.2

### *Ethical Repercussions of Brain-Computer Interfaces (BCIs)*

#### *Objective*

Students will explore and understand the ethical implications of Brain-Computer Interfaces (BCIs) through individual brainstorming, collaborative discussion, and analysis of real-world applications.

#### *Materials Needed*

- Pen and paper or digital devices for note-taking
- Whiteboard or digital collaboration tool (e.g., Google Docs, Jamboard)
- Access to the article ["The ethics of gaming with brain-computer interfaces"](#)



## ***Activity Outline***

### ***Part 1: Individual Brainstorming (15 minutes)***

#### **1. Introduction (5 minutes):**

- Briefly introduce the concept of BCIs and their current and potential applications in various fields such as medicine, gaming, and communication.
- Explain the goal of the activity: to identify and discuss the ethical repercussions of using BCIs.

#### **2. Brainstorming Session (10 minutes):**

- Instruct students to spend 10 minutes listing as many neuro-ethical repercussions of BCIs. Encourage them to consider privacy, consent, security, accessibility, and the potential impact on society.

### ***Part 2: Collaborative Discussion (20 minutes)***

#### **1. Sharing and Combining Lists (15 minutes):**

- Have students pair up or form small groups (3-4 students) and share their lists.
- Each group should combine their lists into a comprehensive list of ethical issues, eliminating duplicates and refining the wording.

#### **2. Class-Wide Discussion (5 minutes):**

- Bring the class together and have each group share their combined list.
- Compile a master list on the whiteboard or a shared digital document, ensuring all unique points are included.

### ***Part 3: Article Reading and Reflection (25 minutes)***

#### **1. Reading the Article (10 minutes):**

- Direct students to read the article ["The ethics of gaming with brain-computer interfaces."](#) They can read individually or in pairs.

#### **2. Reflection and Discussion (15 minutes):**

- After reading, ask students to reflect on the article and identify what surprised them the most.

- Facilitate a class discussion where students share their thoughts and surprising elements from the article.
- Encourage students to compare the ethical issues mentioned in the article with those on the master list created earlier.

#### ***Part 4: Ranking Ethical Issues (20 minutes)***

##### **1. Individual Ranking (5 minutes):**

- Ask students to individually rank the ethical issues listed on the master list from most to least critical based on their perspective.

##### **2. Group Consensus (10 minutes):**

- Form small groups again and have them discuss their rankings.
- Each group should reach a consensus on a ranked list of ethical issues.

##### **3. Class Discussion and Final Ranking (5 minutes):**

- Have each group share their ranked list with the class.
- Facilitate a discussion to create a final class-ranked list of ethical issues, considering the arguments presented by each group.

#### ***Conclusion (5 minutes):***

- Summarize the key points discussed during the activity.
- Highlight the importance of considering ethical implications in neuroengineering and encourage students to continue thinking critically about these issues as they progress in their studies.

#### ***Assessment:***

- Participation in brainstorming, group discussions, and class discussions.
- Quality and depth of the individual and group lists of ethical issues.
- Reflecting thoughtfully on the article and ranking ethical issues,

This activity promotes individual critical thinking, collaborative learning, and the ability to articulate and debate ethical considerations in a scientific context.

---

# Learning Activity 6.3

## *Quescussion on "BCI is Better than BMI"*

### *Objective*

Students will explore the relative merits and limitations of Brain-Computer Interfaces (BCI) and Brain-Machine Interfaces (BMI) through a structured question-based discussion, enhancing their understanding of neuroengineering concepts.

### *Duration:*

20 minutes

### *Materials Needed*

- Whiteboard and markers
- Sticky notes
- Timer

### *Activity Outline:*

#### 1. **Introduction (3 minutes):**

- Briefly introduce BCIs (Brain-Computer Interfaces) and BMIs (Brain-Machine Interfaces), highlighting their definitions, applications, and key differences.
- Explain that BCIs provide a direct communication pathway between the brain and an external device, while BMIs can imply interfaces with machines or robotic systems.

#### 2. **Setup for Quescussion (2 minutes):**

- Explain the rules of the Quescussion:
  - Only questions are allowed. Statements or answers are not permitted.
  - Questions should provoke thought, challenge assumptions, and explore different angles of the topic.
  - Students take turns asking questions, and no question can be repeated.



- If a student accidentally makes a statement, they will be asked to rephrase it as a question or pass their turn.
- Provide each student with sticky notes and a pen.

### 3. **Quescussion (10 minutes):**

- Start the timer for 10 minutes.
- Students take turns asking questions about why BCIs might be considered better than BMIs.
- Encourage students to write down thought-provoking questions on sticky notes and place them on the whiteboard.
- The instructor moderates to ensure adherence to the rules and to keep the discussion focused and dynamic.

### 1. **Reflection and Discussion (3 minutes):**

- Once the Quescussion is complete, review the questions posted on the whiteboard as a class.
- Facilitate a brief discussion where students can make statements and reflect on the questions raised. Encourage them to discuss:
  - Key insights gained from the Quescussion.
  - Which questions were the most challenging or eye-opening?
  - How the activity influenced their understanding of BCIs and BMIs.

### 2. **Conclusion (2 minutes):**

- Summarize the main points discussed.
- Highlight any consensus reached or major differences that remained unresolved.



## Chapter 6: Lab introduction

In this series of lab exercises, you will explore the principles and practical applications of Brain-Computer Interfaces (BCIs) through hands-on activities using MATLAB, Simulink, and Python. These labs will provide you with experience in running and simulating BCI systems, focusing on key processes such as neural activity detection, feature extraction, and classification.

In the first lab, you will utilize MATLAB and Simulink to operate a basic BCI system. This exercise will guide you through essential steps in a typical BCI workflow, including detecting neural activity, amplifying signals, reducing noise, extracting features, and generating output commands. This practical experience will help you understand how BCIs process neural signals to achieve functional outcomes.

In the second lab, you will simulate EEG signals and implement a simple BCI system using Python. The lab will enable you to interactively adjust parameters such as noise levels and stimulation intensity, observing their effects on EEG signals in real-time through a graphical user interface (GUI). This hands-on simulation will enhance your understanding of how feature extraction and classification are applied in BCI systems, providing a comprehensive overview of their functionality and practical use.



## Chapter 6: Lab Example 1



We will use MATLAB and Simulink to run a simple BCI system in this lab example. We will go through the processes of a typical BCI system, such as neural activity detection, amplification, noise reduction, feature extraction, and an output command.

### *Steps*

First, follow this link.

[EEG Feature Extraction Toolbox - File Exchange - MATLAB Central \(mathworks.com\)](https://www.mathworks.com/matlabcentral/fileexchange/78555-EEG-Feature-Extraction-Toolbox)

Download the EEG Feature Extraction Toolbox. Make sure that this toolbox is unzipped and in your MATLAB drive. Then, navigate to the GitHub page for this textbook and go to Chapter 6, Lab Example 1. You will find two MATLAB files: one called `depressed_signals.m` and the other `healthy_signals.m`. You want to download both of those files. Open them in MATLAB and run each of them. This MATLAB script generated artificial EEG signals that produced EEG signals from healthy controls, and then EEG signals that exhibited depression-related features. After this, you should see two variables in your Workspace: `healthy_signals` and `depressed_signals`. These variables in your workspace are essential for the Simulink model to work correctly. Now, navigate to the Home tab and open up Simulink.

Once in Simulink, navigate to the Library Browser and insert the following boxes: two signals from workspace boxes, two Bandpass filter boxes, a MATLAB code box, two scope boxes, and two lamps.

For the two Signal From Workspace boxes, double-click them, and under Signal, type healthy signal for one box and depressed signal for the other. These boxes will take the EEG data generated by the first MATLAB code given at the beginning of the example. You then want to connect one of these boxes to the Bandpass Filter boxes. These filter boxes will clean up the EEG signal and reduce the amount of noise. Double-click your Bandpass Filter Box and set each to the parameters in Fig. 6.5.

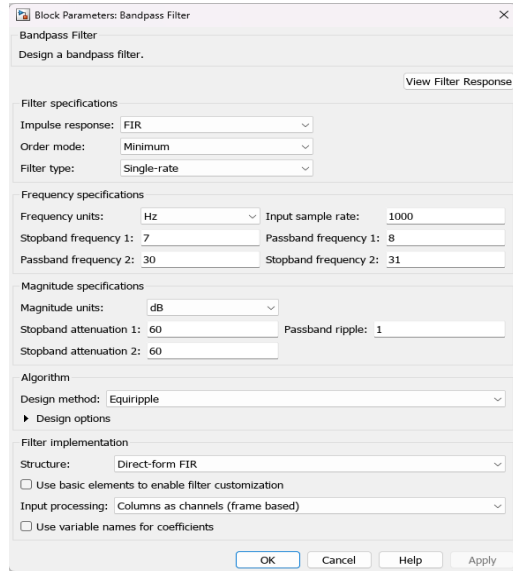


Figure 6.5: Bandpass filter parameters

Then, connect both Bandpass Filter boxes to the MATLAB code box. The MATLAB code box is then attached to each of the scope boxes. In your MATLAB code box, insert the following code.

```
function [healthyPulseControl, depressedPulseControl] =
processEEGAndDeterminePulse(healthy_eeg_data,
depressed_eeg_data)
    % Define opts structure with all necessary fields
    before using it
    opts = struct('fs,' 500, 'alpha,' 2);

    % Process healthy EEG data
    healthyPulseControl =
processSingleEEG(healthy_eeg_data, opts);

    % Process depressed EEG data
```

```

    depressedPulseControl =
processSingleEEG(depressed_eeg_data, opts);
end

function pulseControl = processSingleEEG(eeg_data, opts)
    % Check if jfeeg function is compatible with MATLAB
    Coder.
    % If it's not, you would need to replace it with
    equivalent functionality
    % that is compatible with MATLAB Coder.

    % Hjorth Activity, Mobility, Complexity
    f1 = jfeeg('ha', eeg_data, opts);
    f2 = jfeeg('hm', eeg_data, opts);
    f3 = jfeeg('hc', eeg_data, opts);

    % Feature vector for Hjorth features (not used
    further in this function)
    % hjorth_feat = [f1, f2, f3];

    % Band Power Alpha
    f4 = jfeeg('bpa', eeg_data, opts);

    % Tsallis Entropy
    f5 = jfeeg('te', eeg_data, opts);

    % Define threshold values for determining
    pulseControl
    threshold_activity = 0.1; % Adjust as needed
    threshold_tsallis_entropy = 0.2; % Adjust as needed

    % Evaluate the condition for pulse generation
    pulseControl = (f1 > threshold_activity) && (f5 >
    threshold_tsallis_entropy);
end

```

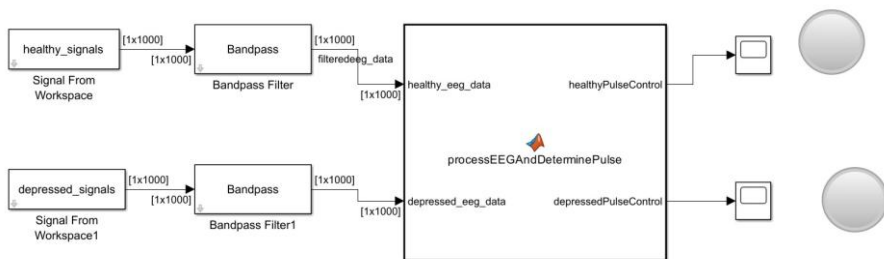


Figure 6.6: Final Simulink Model

This code is the signal processing and feature extraction part of our BCI. This is what your BCI should look like in Simulink. For the lamps, double-click them. Under the Main tab, make sure to have a State of 0, which is the Color red, and a State of 1, which is the Color green. You want to ensure that one lamp is connected to the scope box with the healthyPulseControl variable and the other to the depressedPulsecontrol. To connect the lamp, click the chain icon above the lamp and click on the appropriate scope box. Your final BCI Simulink model should look like Fig. 6.6.

After you have created your Simulink BCI model, select run. Depending on your computer, this simulation may take a few minutes to run, so don't be alarmed if it takes a few minutes. What we expect to see is that our BCI can distinguish between brain activity that is either healthy or exhibits features of depressed neural activity. Once the BCI detects that brain acidity is exhibiting

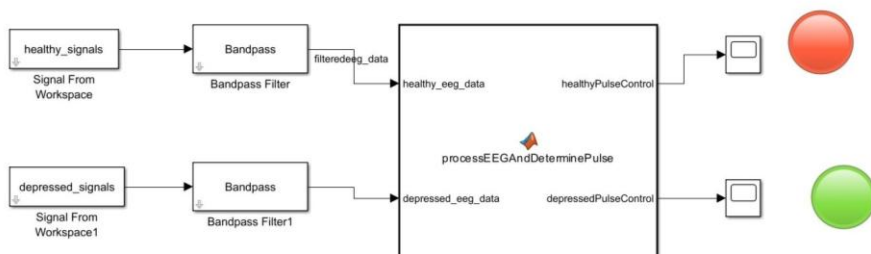


Figure 6.7: Model Results

features of depression, the BCI will generate a neurostimulation impulse to the neurons to try and correct this activity. Our simulation is successful if our healthyPulseControl scope box has no pulse generation and our depressedPulse control does. Additionally, the lamp connected to the depressedPulseControl should light up green when the pulse is delivered, and the other lamp should stay red (fig. 6.7). If this simulation happens too quickly, you can use the Step Forward button to see the color change.

### ***Other Examples and Resources***

Several other examples are available for you to use to keep exploring BCI systems. One includes a hardware example using Muse 2016.

<https://github.com/NeuroTechX/bci-workshop/blob/master/INSTRUCTIONS.md>

For more examples of practical applications of this chapter's content, please visit the book's dedicated GitHub repository page using this link.

[https://github.com/bddupre92/Neurobook\\_BME\\_UND](https://github.com/bddupre92/Neurobook_BME_UND)



# Chapter 6: Lab Example 2

## *EEG Signal Simulation and Classification*



### *Overview*

This lab example demonstrates the simulation of EEG signals, feature extraction, and classification using a simple Brain-Computer Interface (BCI) system implemented in Python. The simulation allows users to interactively modify parameters such as noise level and stimulation intensity and observe their effects on EEG signals in real-time through a graphical user interface (GUI).

### *Goals of the Lab*

- Understand how EEG signals can be simulated and modified to reflect different conditions (healthy vs. depressed).
- Learn how to extract features from EEG signals and classify them using machine learning techniques.
- Gain hands-on experience with a simple BCI system through an interactive GUI.
- Interpret the EEG signal processing results and understand the impact of the different parameters on signal classification.

### *Setup*

#### *Requirements*

- Python 3.8 or later
- The following Python libraries:
  - numpy
  - matplotlib
  - scipy
  - scikit-learn
- Tkinter (usually included with standard Python installations)

#### *Installation*

1. Clone the repository.
2. Navigate to the project directory.

3. Install the required packages:
  - `pip install -r requirements.txt`

### ***Installing Tkinter***

Tkinter is usually included with standard Python installations. If you encounter issues, follow the instructions below:

#### ***Windows***

Tkinter is included with the Python installer on Windows. If not available, reinstall Python using the official installer from [python.org](https://python.org).

#### ***macOS***

Tkinter is included with the Python installation on macOS. If not available, reinstall Python using the official installer from [python.org](https://python.org).

#### ***Linux***

On Debian-based distributions (e.g., Ubuntu):

```
sudo apt-get install python3-tk
```

On Red Hat-based distributions (e.g., Fedora):

```
sudo dnf install python3-tkinter
```

### ***Using the GUI***

#### **Running the GUI**

To run the main script and launch the GUI, execute:

```
python main.py
```

#### **Interacting with the GUI**

1. **Noise Level:** Adjust the level of noise added to the simulated EEG signals. Higher noise levels simulate more real-world conditions with various interferences.
2. **Stimulation Intensity:** Adjust the intensity of the electrical stimulation applied to the EEG signals. Higher intensities can show different patterns in the EEG signals.

After adjusting the parameters, click on **Run Simulation** to generate EEG signals, classify them, and observe the results.

### Meaning of the Parameters

1. Noise Level:
  - Higher noise levels introduce more random variations to the EEG signals, simulating real-world conditions.
  - Lower noise levels produce cleaner signals, making it easier to distinguish between healthy and depressed conditions.
2. Stimulation Intensity:
  - Higher stimulation intensities can significantly alter the EEG signal patterns, making the changes more pronounced.
  - Lower stimulation intensities might show subtler changes in the EEG signals.

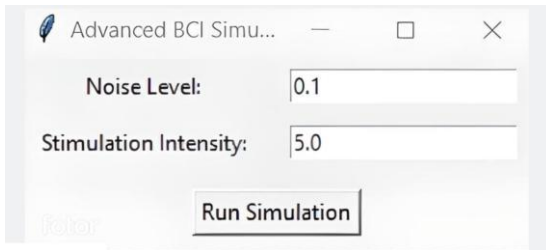


Figure 6.8: Meaning of Parameters

### How This Python Project Relates to BCI

This project simulates a simple BCI system where EEG signals are generated, processed, and classified to determine if they reflect healthy or depressed neural activity. The classification results can then be used to create output commands, such as stimulating neurons to correct detected anomalies in brain activity. This hands-on experience helps me understand the basic components and functioning of BCIs.

### File Structure

3. **simulate\_eeg.py**: Contains functions to generate and plot simulated EEG signals.

4. **extract\_features.py**: Contains functions to extract features from EEG signals and train a classifier.
5. **generate\_output.py**: Contains functions to generate output commands based on classifier predictions.
6. **bci\_gui.py**: Contains the GUI for interactive parameter adjustment.
7. **main.py**: Launches the GUI for interactive use.
8. **requirements.txt**: Lists all necessary packages to run the scripts.
9. **README.md**: Provides instructions for setting up and running the project.

### Interpretation of Results

- **EEG Signal Plots**: The GUI plots the EEG signals for healthy and depressed conditions. Differences in amplitude and patterns can indicate variations in neural activity.
- **Classifier Accuracy**: The accuracy of the classifier in distinguishing between healthy and depressed EEG signals is displayed. Higher accuracy indicates a better-performing classifier.
- **Output Commands**: The generated output commands based on the classifier's predictions are shown. "Stimulate" indicates the detection

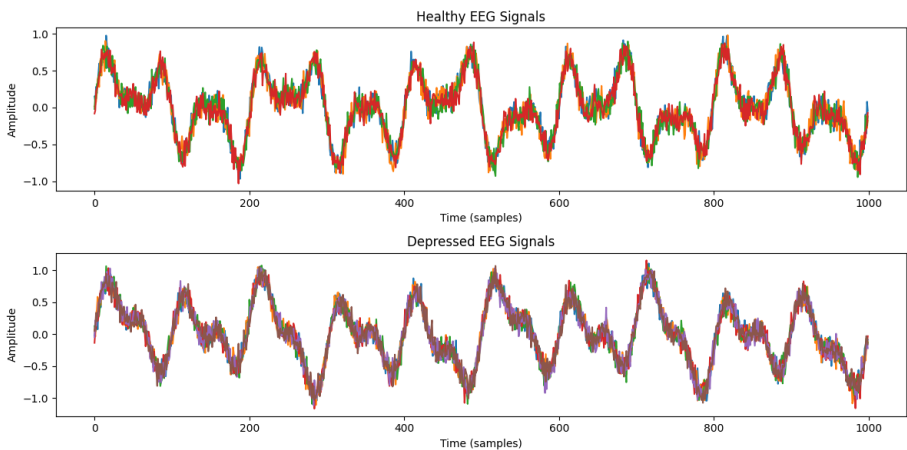


Figure 6.9: Healthy vs Depressed EEG Signals

of depressed neural activity requiring intervention, while "No Stimulate" indicates healthy activity.

### Suggestions for Parameters to Modify

#### *Noise Level:*

- Increasing the noise level will make it harder for the classifier to distinguish between healthy and depressed signals, simulating more challenging real-world conditions.
- Decreasing the noise level will produce cleaner signals, making it easier for the classifier to perform accurately.
- Stimulation Intensity:
  - Higher intensities can lead to more pronounced changes in the EEG signals, helping to understand the effect of different stimulation strengths.
  - Lower intensities show subtler effects, which is useful for studying the minimal effective stimulation required for therapeutic effects.

By exploring these parameters and their impacts on the EEG signals and classifier performance, users can gain deeper insights into the dynamics of neural activity and the potential of BCIs in clinical and research settings.





## Chapter 7

# Electrifying Insights in Neurostimulation

# Introduction and Learning Objectives

Neurostimulation technologies have become essential tools in treating various neurological disorders. By directly interacting with the nervous system, these technologies offer new ways to manage conditions that were previously difficult to treat with conventional therapies. This chapter will explore two prominent neurostimulation techniques: Transcranial Magnetic Stimulation (TMS) and Deep Brain Stimulation (DBS). By the end of this chapter, you will be able to:

- 1. Understand the Importance of Neurostimulation Technologies: Recognize the crucial role of neurostimulation technologies in managing conditions resistant to conventional therapies.*
- 2. Describe the Components and Function of TMS and DBS Systems: Identify and explain the critical hardware components and setup processes for TMS and DBS systems.*
- 3. Utilize TMS and DBS Software Tools: Gain knowledge about the software tools for programming stimulation patterns, ensuring safety, and tracking patient responses in both TMS and DBS.*
- 4. Evaluate the Advantages and Disadvantages of TMS and DBS: Assess the pros and cons of TMS and DBS, considering factors such as non-invasiveness, effectiveness, and potential risks.*
- 5. Discuss the Current State of the Art and Future Directions in Neurostimulation: Stay informed about the latest advancements, ethical considerations, and potential new applications in neurostimulation technologies.*

## Importance of Neurostimulation Technologies in Treating Neurological Disorders

Neurostimulation technologies are revolutionizing the field of neurology by providing treatments for a diverse range of disorders, including depression, epilepsy, Parkinson's disease, and chronic pain. These innovative technologies modulate neural activity, offering the unique advantage of restoring normal brain function or alleviating symptoms. Their significance is underscored by their ability to provide minimally invasive, targeted treatments with

significantly fewer side effects than traditional drug therapies. This makes neurostimulation technology particularly valuable for patients who do not respond well to conventional therapies or experience severe side effects, ultimately improving patient outcomes [167].

### ***Overview of TMS and DBS***

Transcranial Magnetic Stimulation (TMS) and Deep Brain Stimulation (DBS) are two widely used neurostimulation techniques with unique mechanisms and applications. TMS is a non-invasive procedure that employs magnetic fields to stimulate nerve cells in the brain. It is primarily used for treating major depressive disorder, with ongoing research into its effectiveness for anxiety, stroke rehabilitation, and migraines. During TMS, an electromagnetic coil against the scalp generates magnetic pulses that induce electrical currents, modulating neuronal activity in specific brain regions [168]. On the other hand, DBS involves surgically implanting electrodes into precise areas of the brain. These electrodes are connected to a pulse generator in the chest that delivers electrical impulses. This method is commonly used to treat movement disorders such as Parkinson's disease, essential tremor, and dystonia. It has shown promise in managing psychiatric conditions like obsessive-compulsive disorder and depression [167]. Although DBS is more invasive than TMS, it offers the advantage of continuous, adjustable stimulation. Both TMS and DBS are significant advancements in neuroengineering, providing powerful tools to modulate brain activity and improve patient outcomes, marking a substantial impact on modern neurotherapeutics [169].

## **Transcranial Magnetic Stimulation (TMS)**

Transcranial Magnetic Stimulation (TMS) is a non-invasive technique that uses magnetic fields to stimulate nerve cells in the brain. This section delves into the hardware and software components of TMS systems, their setup and configuration, and the advantages and disadvantages of TMS.

## TMS Mechanism

TMS generates magnetic fields that penetrate the scalp and skull to induce electrical currents in specific brain areas. The TMS coil, typically in a figure-eight shape, is positioned over the target brain region. When activated, the coil generates a magnetic field that induces electric currents in the cortical neurons, leading to neuronal activation or inhibition.

While TMS can stimulate motor pathways, as seen when a corticospinal volley activates spinal motoneurons to produce an action potential in the peripheral nerve, it can also target other types of nerve cells involved in various brain

**Simplified scheme of mechanism of action of TMS of the motor cortex**

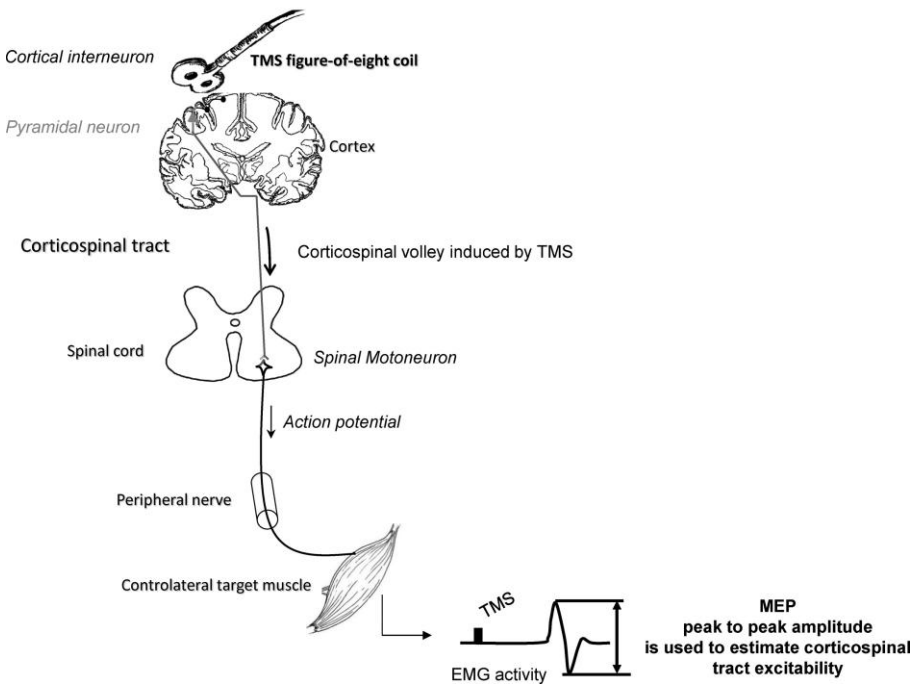


Figure 7.1: Simplified scheme of the mechanism of action of TMS on the motor cortex. The TMS coil generates a corticospinal volley that travels through the corticospinal tract, activating spinal motor neurons and induces an action potential in the peripheral nerves, leading to muscle activation. This mechanism underlies the therapeutic effects of TMS. [171]

functions, depending on the stimulation site and parameters. The action potential ultimately leads to muscle activation in the contralateral target muscle [170]. Fig. 7.1 [171] provides a simplified overview of the TMS mechanism of action, focusing on the motor cortex. This process underlies the therapeutic effects of TMS in various neurological and psychiatric conditions, providing a non-invasive method to modulate brain activity and improve patient outcomes.

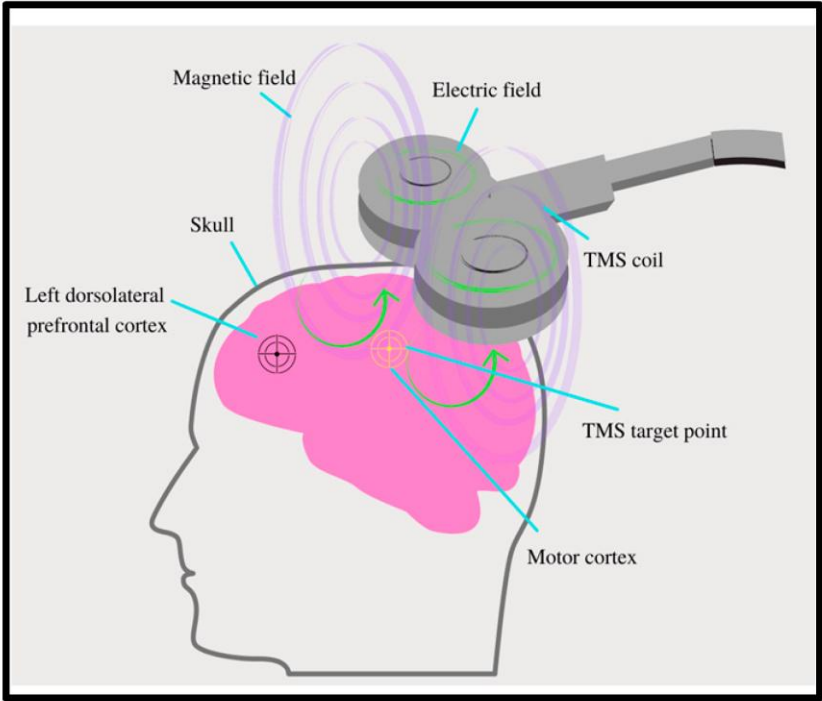


Figure 7.2: Components of TMS [172]

***TMS Hardware***

TMS systems have several key components that deliver precise magnetic stimulation to targeted brain regions. The main components include the pre-planning and control unit, which is responsible for planning the stimulation parameters and controlling the overall operation of the TMS system. This unit

interfaces with the signal generator and the positioning system to ensure accurate delivery of the magnetic pulses [168].

TMS systems have several key components that deliver precise magnetic stimulation to targeted brain regions. The main components include the pre-planning and control unit, signal generator, positioning system, magnetic coil, and stereo vision camera. The pre-planning and control unit is responsible for planning the stimulation parameters and controlling the overall operation of the TMS system. This unit interfaces with the signal generator and the positioning system to ensure accurate delivery of the magnetic pulses. The signal generator generates the electrical signals that drive the magnetic coil. This component can produce pulses of varying intensity and frequency, which is crucial for therapeutic applications. Accurate positioning of the magnetic coil is essential for effective stimulation, and the positioning system, often guided by a stereo vision camera, ensures that the coil is placed at the correct location and orientation relative to the patient's head. The magnetic coil is the core component of the TMS system. It generates magnetic fields that penetrate the scalp and skull to reach the underlying brain tissue. The figure-eight coil design is commonly used for its ability to focus the magnetic field on a specific brain region. Additionally, the stereo vision camera assists in precise coil positioning by providing real-time visual feedback to the positioning system, helping to maintain the coil's correct placement during the TMS session. Fig. 7.2 [172] illustrates the interaction between these components.

### ***Setup and Configuration***

The setup and configuration of a TMS system involve several steps to ensure accurate and effective stimulation (Fig. 7.3 [170]). The clinician inputs the desired stimulation parameters into the control unit, including the intensity, frequency, and duration of the magnetic pulses. Using the stereo vision camera and positioning system, the clinician accurately places the magnetic coil over the targeted brain region, ensuring the coil maintains the correct orientation and distance from the scalp [168].

The signal generator then produces the electrical signals that drive the coil, generating magnetic pulses that stimulate the underlying brain tissue and

modulate neuronal activity in the targeted area. Throughout the session, the clinician monitors the patient's response and makes any necessary adjustments to the stimulation parameters to optimize the therapeutic effect.

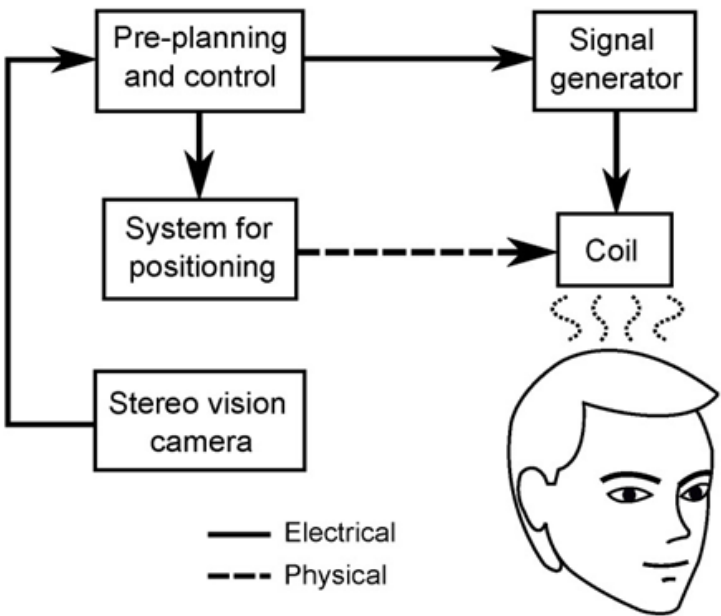


Figure 7.3: Block diagram of TMS hardware setup showing the interaction between the pre-planning and control unit, signal generator, positioning system, magnetic coil, and stereo vision camera [170]

***TMS Software***

TMS software is crucial in ensuring the precise and safe administration of magnetic stimulation. The software includes signal processing tools, analysis software, and patient response tracking mechanisms. The signal processing tools are essential for programming the stimulation patterns, ensuring safety, and conducting compliance checks. These tools allow clinicians to set the intensity, frequency, and duration of the magnetic pulses. Safety features are

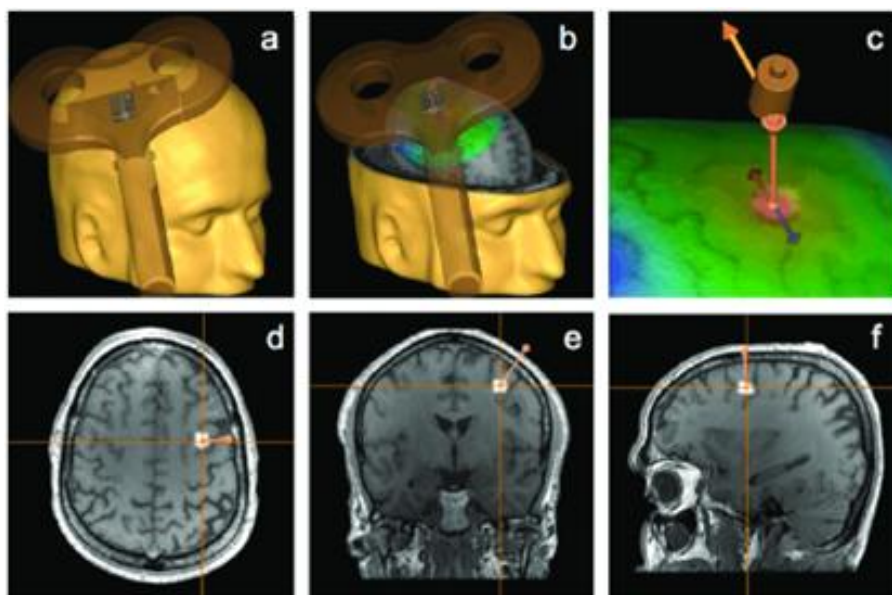


Figure 7.4: TMS-targeted region neuronavigation and coil placement. The specific location of the TMS coil relative to the targeted brain region is shown using MRI guidance. a) 3D model of the head with the TMS coil positioned. b) Coil placement relative to the brain's surface. c) MRI-guided targeting of the brain region for TMS. d) Coronal MRI slice showing the TMS target area. e) Axial MRI view showing coil alignment with the brain target. f) Sagittal MRI slice demonstrating coil position relative to the brain. [169]

integrated to monitor the parameters continuously, ensuring they remain within safe limits to prevent adverse effects.

TMS systems often integrate analysis software with imaging software to provide a comprehensive view of brain activity. This integration allows for the creation of detailed maps of brain regions, facilitating targeted stimulation [173]. The analysis software processes data from imaging techniques such as MRI or CT scans to identify the precise locations for stimulation, enhancing the accuracy and effectiveness of the treatment. The following image (Fig. 7.4 [169]) illustrates TMS-targeted region neuronavigation and coil placement, showing the specific location of the TMS coil relative to the targeted brain region using MRI guidance.

Patient response tracking software monitors and records the patient's responses to stimulation. This software collects data on various parameters, including

motor-evoked potentials (MEPs) and other physiological responses. The data is analyzed to assess the treatment's effectiveness and make any necessary adjustments to the stimulation parameters. This continuous feedback loop helps optimize the therapy for individual patients. These software tools ensure that TMS treatments are administered accurately, safely, and effectively, tailored to each patient's needs[168].

***Advantages and Disadvantages of TMS***

The table below provides a detailed comparison of the advantages and disadvantages of TMS [169]:

| Advantages                                                                                                                                                                                                                                                                                                                                                      | Disadvantages                                                                                                                                                                                                                                                           |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Noninvasive, outpatient treatment</b><br><br>TMS does not require surgery or anesthesia, making it a less invasive option than other neurological treatments like Deep Brain Stimulation (DBS). Patients can receive TMS treatment in an outpatient setting without hospitalization, allowing them to resume daily activities immediately after the session. | <b>Limited penetration depth</b><br><br>The magnetic fields generated by the TMS coil can only penetrate a few centimeters into the brain, limiting the treatment to superficial cortical areas and making it less effective for deeper brain structures.               |
| <b>High temporal resolution</b><br><br>TMS allows for precise timing of stimulation, which is crucial for understanding and modulating brain functions that occur on a millisecond scale. This high temporal resolution enables researchers and clinicians to study                                                                                             | <b>Requires multiple sessions for effect</b><br><br>Effective treatment with TMS often requires a series of sessions over several weeks. This can be time-consuming and may require significant commitment from patients. Additionally, the cumulative cost of multiple |

|                                                                                                                                                                                                |                                                                                                                                                                                                                                                |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| the brain's dynamic processes and apply targeted therapies.                                                                                                                                    | sessions can be a financial burden.                                                                                                                                                                                                            |
| <b>Minimal side effects</b>                                                                                                                                                                    | <b>Variable response among patients</b>                                                                                                                                                                                                        |
| Compared to pharmacological treatments, TMS has fewer side effects, the most common being mild scalp discomfort or headache, which typically resolves shortly after the session.               | The efficacy of TMS can vary significantly among patients, with some experiencing substantial benefits while others may see minimal improvement. This variability can make it challenging to predict treatment outcomes.                       |
| <b>Ability to target specific brain regions</b>                                                                                                                                                | <b>Limited long-term data</b>                                                                                                                                                                                                                  |
| TMS can be precisely targeted to specific brain regions involved in various neurological and psychiatric disorders, allowing for focused treatment that minimizes impact on other brain areas. | While TMS has shown promise in treating certain conditions, there is still limited long-term data on its efficacy and safety, particularly for newer indications. Further research is needed to understand the long-term effects of TMS fully. |
| <b>Non-pharmacological treatment option</b>                                                                                                                                                    | <b>Initial setup and calibration required</b>                                                                                                                                                                                                  |
| TMS provides an alternative to medication, which is particularly beneficial for patients who do not respond well to drugs or experience adverse effects from them.                             | The initial setup and calibration of the TMS machine require specialized knowledge and can be time-consuming. Proper coil positioning and adjustment of stimulation parameters are crucial for effective treatment.                            |

# Deep Brain Stimulation (DBS)

Deep Brain Stimulation (DBS) is an invasive neuromodulation technique that involves implanting electrodes into specific brain regions to modulate neural activity. This section explores the mechanism behind DBS using the provided image.

## *DBS Mechanism*

DBS delivers continuous electrical impulses to targeted areas in the brain through implanted electrodes. These impulses modulate neural activity, providing therapeutic benefits for neurological and psychiatric disorders [167]. Fig. 7.5 [174] illustrates the complex mechanism of action of DBS:

1. **Entrainment of Axonal Orthodromic Action Potentials (APs):** DBS electrodes deliver electrical pulses that entrain axonal orthodromic APs, leading to consistent and patterned neural activity.
2. **Antidromic APs Collide with Intrinsic Orthodromic APs:** The electrical stimulation generates antidromic APs, which travel backward along the axon. These antidromic APs can collide with the naturally occurring orthodromic APs, altering the overall activity of the neuron.
3. **Excitation of Afferent Inhibitory and Excitatory Fibers Projecting to Target Neurons:** The stimulation excites inhibitory and excitatory afferent fibers that project to the target neurons, modulating their activity.
4. **Excitation of Passing Fibers Projecting to the Targets:** DBS can also affect passing fibers that project to other targets, influencing neural circuits beyond the immediate vicinity of the electrode.
5. **Neurotransmitter Release:** The electrical impulses stimulate neurotransmitter release, which can enhance or inhibit synaptic transmission, depending on the neurotransmitters involved.
6. **Microenvironmental Effects on Non-Neuronal Cells:** DBS impacts the microenvironment, affecting non-neuronal cells such as astrocytes and microglia, which play critical roles in maintaining neural health and modulating synaptic activity.

7. Effects on Blood-Brain Barrier: The stimulation can influence the permeability of the blood-brain barrier, potentially affecting the movement of molecules between the bloodstream and the brain.

DBS provides therapeutic benefits by precisely modulating neural circuits involved in various disorders. Understanding these mechanisms helps optimize DBS settings and improve patient outcomes.

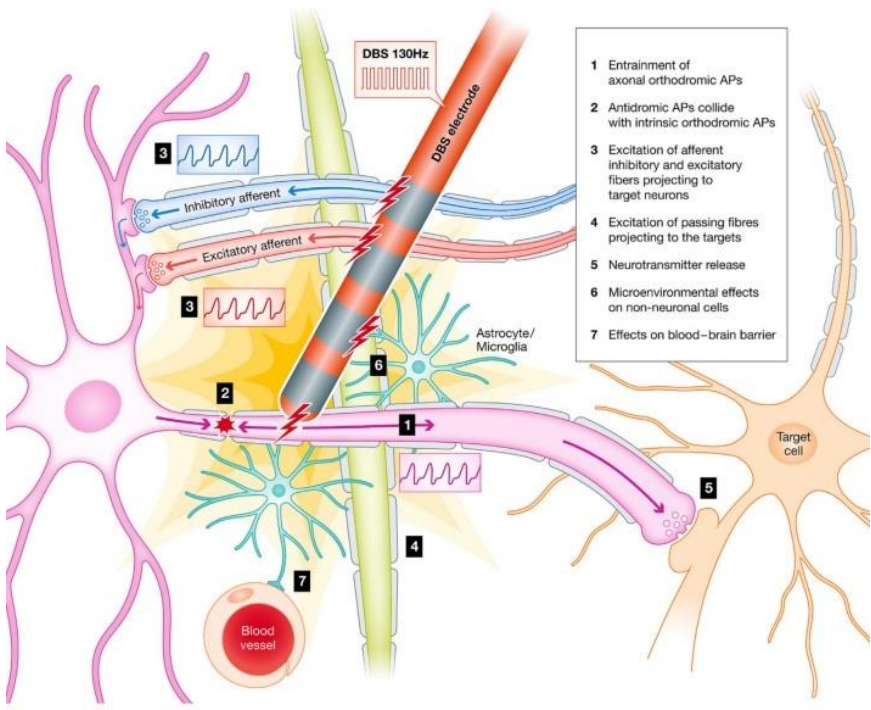


Figure 7.5: The mechanism of action of DBS, showing the electrode delivering electrical stimulation and its effects on neuronal and non-neuronal cells. [174]

### DBS Hardware

DBS systems have several key components that deliver precise electrical stimulation to targeted brain regions. The main components include electrodes, lead wires, implantable pulse generators (IPGs), and extension cables (Fig. 7.6 [175]).

The electrodes are designed to be implanted in specific brain regions associated with the disorder being treated. They are typically made of biocompatible materials and feature multiple contacts that allow for precise stimulation of target areas [169]. The IPG, also known as the neurostimulator, is implanted in the chest or abdomen and generates the electrical pulses delivered to the brain through the electrodes. The IPG can be programmed to adjust the stimulation's frequency, intensity, and duration to optimize therapeutic outcomes [173].

The setup and implantation of a DBS system involve a multi-step surgical procedure. Initially, a neurosurgeon creates a small opening in the skull to insert the electrodes into the targeted brain region. The exact placement is guided by advanced imaging techniques and neurophysiological mapping to ensure precision. After the electrodes are implanted, the lead wires are tunneled under the skin to connect with the IPG, which is placed in a subcutaneous pocket in the chest or abdomen. Following the surgery, the IPG is programmed and adjusted based on the patient's response to the stimulation. Regular follow-up visits are necessary to fine-tune the settings and ensure optimal therapeutic benefits.

By understanding DBS systems' components and setup process, clinicians can effectively utilize this technology to treat various neurological and psychiatric disorders, enhancing patient outcomes and quality of life.

### ***DBS Software***

DBS software plays a crucial role in managing and optimizing DBS therapy. The software includes programming tools, remote monitoring and adjustments, and data management systems [173].

The programming tools in DBS software are essential for customizing the stimulation parameters, ensuring the therapy is tailored to each patient's specific needs. Clinicians can adjust the frequency, intensity, and duration of the electrical pulses and the configuration of the electrode contacts. This level of customization is critical for achieving optimal therapeutic outcomes and minimizing side effects, allowing for precise targeting of the affected brain areas [173].

Remote monitoring and adjustments are another critical feature of DBS software. Clinicians can remotely access the DBS system to monitor the patient's status and make necessary real-time adjustments. This capability enhances the therapy's flexibility and responsiveness, ensuring patients receive continuous and effective treatment. It also allows for timely interventions

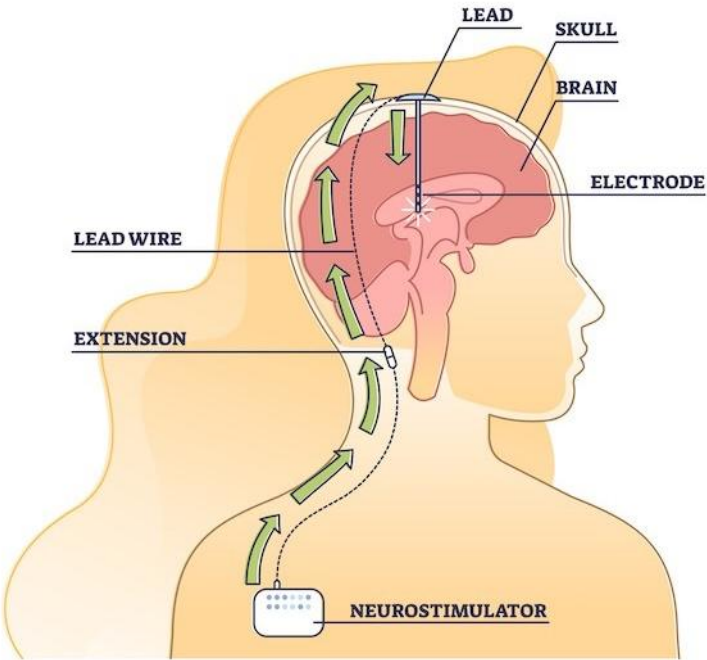


Figure 7.6: Components of a DBS system, including the electrode, lead wire, extension, and neurostimulator. [175]

without the need for frequent in-person visits, improving the overall management of the therapy.

The software includes robust data management tools for recording and analyzing patient data. It tracks various parameters, including the settings of the stimulation, the patient's physiological responses, and any adverse effects. This data is crucial for evaluating the effectiveness of the therapy and making informed decisions about adjustments. Additionally, the software incorporates safety protocols and error detection features to ensure the system operates within safe limits and promptly identifies potential issues. By integrating these advanced data management capabilities, DBS therapy can be effectively monitored and optimized, providing significant benefits for patients with neurological and psychiatric disorders [173].

***Advantages and Disadvantages of DBS***

The table below provides a detailed comparison of the advantages and disadvantages of Deep Brain Stimulation (DBS):

| Advantages                                                                                                                                | Disadvantages                                                                                                                                            |
|-------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Effective for treatment-resistant disorders</b>                                                                                        | <b>Invasive with potential surgical risks</b>                                                                                                            |
| DBS is highly effective for disorders that do not respond to conventional treatments, providing relief where other therapies have failed. | The procedure involves surgery, which carries inherent risks such as infection, bleeding, or adverse reactions to anesthesia.                            |
| <b>Direct stimulation allows for targeted treatment.</b>                                                                                  | <b>High cost and need for periodic battery replacements.</b>                                                                                             |
| High cost and need for periodic battery replacements                                                                                      | The high cost of the DBS system and the need for periodic replacements of the battery in the neurostimulator can be financially burdensome for patients. |

|                                                                                                                                                                  |                                                                                                                                                            |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Adjustable and reversible therapy</b>                                                                                                                         | <b>Potential for hardware complications</b>                                                                                                                |
| The stimulation parameters can be adjusted to optimize therapeutic outcomes and minimize side effects, and the system can be turned off or removed if necessary. | There is a risk of hardware-related issues such as lead migration, device malfunction, or breakage, which may require additional surgeries to correct.     |
| <b>Improves quality of life and daily functioning</b>                                                                                                            | <b>Possible side effects and complications</b>                                                                                                             |
| Many patients experience significant improvements in symptoms, leading to better quality of life and increased ability to perform daily activities.              | Potential side effects include speech problems, balance issues, or changes in mood or behavior, which may require adjustments to the stimulation settings. |
| <b>Potential for reduced medication use</b>                                                                                                                      | <b>Long recovery and adjustment period</b>                                                                                                                 |
| DBS can reduce the need for medications, thereby decreasing the side effects and risks associated with long-term drug use.                                       | Recovery from surgery and adjustment to the DBS system can be lengthy and may require several visits for tuning and optimization.                          |

## Current State of the Art

### *Innovations in Neurostimulation*

Recent advancements in neurostimulation have significantly enhanced the efficacy and safety of treatments like TMS and DBS. One of the latest developments is the improvement in electrode technology, which has led to more precise and effective stimulation with fewer side effects. Advanced materials and designs enable better targeting of specific brain regions, improving therapeutic outcomes.

Software algorithms have also substantially improved, providing more sophisticated programming tools for highly individualized treatment plans. These algorithms can adjust stimulation parameters in real-time, optimizing therapy based on patient responses. Integrating artificial intelligence (AI) and real-time monitoring systems further enhances the ability to tailor treatments, providing continuous feedback and adjustments that improve overall effectiveness.

Another exciting innovation is the development of noninvasive DBS techniques. While traditional DBS requires the surgical implantation of electrodes, research explores methods to deliver similar therapeutic benefits without invasive procedures. These noninvasive approaches could reduce the risks associated with surgery and make neurostimulation therapies accessible to a broader range of patients [176].

### ***Challenges and Future Directions***

Despite these advancements, several challenges remain in the field of neurostimulation. Ethical considerations are paramount, particularly concerning the long-term effects of brain stimulation and the potential for misuse. Ensuring patient safety and informed consent is critical as these technologies evolve and are widely used.

New neurostimulation applications in treating neurological and psychiatric disorders also have significant potential. Ongoing research explores how these technologies can be adapted to address a broader range of conditions, including those currently challenging to treat with existing therapies [177]. This includes investigating the underlying mechanisms of neurostimulation to understand better how it affects brain function and developing more effective and targeted treatments.

## **Chapter 7: Summary**

Neurostimulation technologies like TMS and DBS have had a profound impact on modern medicine, offering new hope for patients with treatment-resistant neurological and psychiatric disorders. These therapies provide targeted,

effective treatments with fewer side effects than traditional methods, improving the quality of life for many individuals.

The importance of ongoing research and development in this field cannot be overstated. Continued advancements in electrode technology, software algorithms, and non-invasive techniques will enhance the efficacy and safety of neurostimulation therapies. Additionally, addressing ethical considerations and expanding the range of treatable conditions will be crucial for the future of neurostimulation. By fostering innovation and rigorous research, the potential of these life-changing technologies can be fully realized, offering better outcomes for patients worldwide.



# Chapter 7: Learning Activities

## Learning Activity 7.1

### *Learning Activity: Create a Concept Map for a TMS Machine*



#### ***Objective***

Students will individually and collaboratively create a concept map connecting and explaining a TMS machine's various parts and functions.

A concept map is a visual representation tool used to organize and structure knowledge by displaying relationships among concepts in a graphical format. It typically consists of nodes, points, or circles representing individual concepts or ideas, and links, which are lines connecting the nodes to illustrate relationships. These links often include words or phrases specifying the nature of the relationship, such as "causes," "includes," or "is part of." Concept maps usually have a hierarchical structure, with the most general concepts at the top and more specific details below, highlighting levels of abstraction and the flow of information. Key features of concept maps include a central concept, branches for subtopics or related concepts, and cross-links that show relationships between different segments, helping to illustrate interconnected knowledge areas. Concept maps are useful for organizing information, aiding learning and teaching by breaking down complex information into manageable parts, facilitating brainstorming, assisting in problem-solving by identifying relationships and dependencies, and planning projects by outlining key components and their relationships. For example, a concept map for a TMS machine might have "TMS Machine" as the central node, with branches for components like the coil, pulse generator, cooling system, user interface, and power supply, each with sub-nodes detailing specific attributes and functions. This structured, visual approach makes concept maps an effective tool for understanding and remembering complex topics.

#### ***Materials Needed***

- Large sheets of paper or whiteboard

- Markers or pens
- Sticky notes (optional)
- Reference materials on TMS machines (textbooks, diagrams, online resources)
- Concept mapping software (optional, e.g., MindMeister, Coggle)

### ***Preparation (Before Class)***

**Assignment:** Students are assigned to research the TMS machine, its components, and their functions before class. They should come prepared with notes and basic understanding.

### ***Stage 1: Individual Work (10 minutes)***

1. **Individual Concept Map Creation:**
  - **Work Time (10 minutes):** Students work individually to draft their concept maps. They start with the central node (TMS machine) and create branches for each main component, adding sub-branches and connections as they see fit based on their pre-class research.

### ***Stage 2: Collaborative Work***

#### ***Step 1: Pairs (10 minutes)***

1. **Form Pairs:**
  - **Pair Up:** Students pair up to compare their concept maps.
2. **Combine and Improve:**
  - **Discussion (5 minutes):** Each pair discusses their maps, noting similarities and differences.
  - **Merged Map (5 minutes):** Together, they create a combined concept map that incorporates the best elements from both individual maps, ensuring all components are accurately represented and well-connected.

#### ***Step 2: Groups of Three (15 minutes)***

1. **Form Groups of Three:**

- **Combine Pairs:** Each pair joins another student or another pair to form a group of three.
- 2. **Refine and Expand:**
  - **Discussion (5 minutes):** Each group member presents their combined maps, discussing key points and connections.
  - **Unified Map (10 minutes):** The group creates a final, unified concept map that integrates input from all members. They refine connections, add missing details, and ensure clarity and accuracy.

### ***Debrief to the Class (15 minutes)***

1. **Group Presentations:**
  - **Presentation (2 minutes per group):** Each group presents their concept map to the class, explaining their connections and how they decided on the final structure.
2. **Class Discussion:**
  - **Feedback (3 minutes):** After each presentation, allow time for questions and feedback from peers and the instructor.
3. **Reflection:**
  - **Facilitated Discussion (5 minutes):** Engage the class in a discussion about what they learned from the activity. Ask students how working individually and then collaboratively helped them understand the TMS machine better.
  - **Key Takeaways:** Summarize the main points and correct any misconceptions.

### ***Assessment***

- **Completeness:** Ensure all key components and their relationships are included.
- **Accuracy:** Verify that the information and connections accurately represent the TMS machine.
- **Clarity:** Evaluate the clarity and readability of the concept maps.
- **Collaboration:** Observe the effectiveness of collaboration in pairs and groups of three.
- **Presentation:** Assess the effectiveness of each group's presentation and their ability to explain their concept map.

## *Exit Ticket:*

- **Individual Reflection:** Before leaving, each student completes an exit ticket that includes the following questions:
  1. **Key Insight:** What is one new thing you learned about the TMS machine today?
  2. **Collaboration Benefit:** How did collaborating with your peers enhance your understanding of the TMS machine?
  3. **Personal Contribution:** What was your most significant contribution to your group's concept map?
  4. **Remaining Questions:** Do you have any remaining questions or areas of confusion about the TMS machine?

By including an exit ticket, students can reflect on their learning, provide feedback on the collaborative process, and identify areas where they might need further clarification. Learning activity 7.2

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## **Learning Activity 7.2**

### ***Understanding Deep Brain Stimulation (DBS)***

#### ***Objective***

Students will enhance their understanding of Deep Brain Stimulation (DBS) by watching an informative video, participating in a collaborative discussion using the "yes, and..." technique, and ensuring every student has the opportunity to speak.

#### ***Materials Needed***

- Projector and computer to show the video
- Internet access to watch the YouTube video
- Whiteboard and markers
- Timer



## *Activity Steps*

### 1. Watch the Video (10 minutes):

- **Introduction:** Briefly introduce the topic of Deep Brain Stimulation and its importance in medical science.
- **Video Viewing:** Watch the YouTube video "Deep Brain Stimulation" in class.
  - [Deep Brain Stimulation Video](#)

### 2. Collaborative Discussion: "Yes, and..." Technique (30 minutes):

- **Explain the Technique:** Briefly explain the "yes, and..." technique. Each student should build on the previous student's comment by responding with "yes, and...". This promotes active listening and collaborative thinking.
- **Discussion Topics:**

#### 1. What impressed you the most about DBS?

#### 2. Which parameters can you change in DBS stimulation?

- **Participation Rule:** Introduce the "1/x" rule, where "x" is the number of students in the class. This means each student gets approximately 1/x of the total discussion time, ensuring everyone has a chance to speak.

### 3. Discussion Facilitation:

- **Assign Roles:** Designate a discussion facilitator to keep track of time and ensure everyone follows the "yes, and..." technique. The facilitator can also prompt students who haven't spoken yet.
- **Round-Robin Format:** Start the discussion in a round-robin format to ensure each student has an equal chance to speak. Encourage students to build on each other's comments using "yes, and..."
- **Whiteboard Notes:** Use the whiteboard to jot down key points from the discussion, highlighting the most impressive aspects of DBS and the parameters that can be adjusted.

### 4. Debrief and Reflection (10 minutes):

- **Summary:** Summarize the main points discussed, highlighting what impressed students the most and the key parameters of DBS that can be changed.
- **Reflection Questions:** Ask students to reflect on the discussion process and their learning:

- What new insights did you gain about DBS?
- How did the "yes, and..." technique affect the discussion?
- What did you learn from your classmates' contributions?

#### 5. Exit Ticket (5 minutes):

- **Individual Reflection:** Each student completes an exit ticket answering the following questions:
  1. What is one new thing you learned about DBS today?
  2. How did the "yes, and..." technique help you in the discussion?
  3. What is one question you still have about DBS?

#### *Assessment:*

- **Participation:** Ensure each student contributes to the discussion using the "yes, and..." technique.
- **Understanding:** Evaluate students' knowledge of DBS based on their contributions and exit tickets.
- **Collaboration:** Assess how well students build on each other's ideas and work together to explore the topic. Learning activity 7.3

## Learning Activity 7.3

### *Exploring TMS vs. BCI through Quescussion*

#### *Objective*

Students will critically evaluate and discuss the merits and drawbacks of Transcranial Magnetic Stimulation (TMS) and Brain-Computer Interfaces (BCI) through structured Quescussion.

#### *Materials Needed:*

- Whiteboard and markers



- Timer

### ***Activity Steps:***

#### **1. Introduction (5 minutes):**

- **Context Setting:** Briefly introduce TMS and BCI, highlighting their primary uses and differences. Explain that today's activity will involve a Quescussion—a type of discussion where only questions are allowed.

#### **2. Edgy Statement (5 minutes):**

- **Present the Statement:** Write the following on the board: "TMS is better than BCI."
- **Explain Quescussion:** Inform students that they can only respond to the statement with questions. The goal is to explore the topic deeply through inquiry, challenging assumptions, and uncovering different perspectives.

#### **3. Quescussion Activity (15 minutes):**

- **Rules and Roles:**
  - No statements, only questions are allowed.
  - Encourage every student to participate. Use a timer to ensure equal participation.
  - Designate a scribe to write down key questions on the board.
- **Begin the Quescussion:**
  - If needed, prompt with an initial question: "What makes TMS better than BCI?"
  - Allow students to build on each other's questions, maintaining the inquiry flow.

#### **4. Facilitation and Participation:**

- **Monitor Participation:** Ensure that all students are asking questions and that the discussion remains focused. Use the 1/x rule to remind students that everyone should have equal time to contribute.

- **Encourage Depth:** Prompt students to ask deeper, more probing questions: "How do the long-term effects of TMS compare to those of BCI?" or "What specific applications of TMS might be considered superior to BCI?"
5. **Transition to Open Discussion (10 minutes):**
- **End of Quescussion:** After 15 minutes, transition to an open discussion. Allow students to start making statements and building on the questions raised during the Quescussion.
  - **Discussion Points:**
    - What were the most compelling questions raised?
    - How do the advantages and disadvantages of TMS and BCI compare?
    - Which scenarios or applications might make one technology preferable over the other?
6. **Debrief and Reflection (10 minutes):**
- **Summary of Key Points:** Summarize the main questions and insights from the Quescussion and subsequent discussion.
  - **Reflective Questions:**
    - What did you learn about TMS and BCI that you didn't know before?
    - How did the Quescussion format influence your thinking about the topic?
    - Do you feel more informed about the strengths and weaknesses of TMS and BCI?
7. **Exit Ticket (5 minutes):**
- **Individual Reflection:** Each student completes an exit ticket answering the following questions:
    1. What is one significant question you have about TMS or BCI after today's activity?
    2. How did the Quescussion format help you understand the topic better?
    3. Based on today's discussion, which technology do you think holds more promise for the future, TMS or BCI, and why?

### ***Assessment:***

- **Participation:** Ensure each student asks questions and engages in the Quescussion and open discussion.
- **Critical Thinking:** Evaluate the depth and relevance of the questions asked during the Quescussion.
- **Understanding:** Assess students' understanding of TMS and BCI based on their contributions and exit tickets.
- **Reflection:** Review exit tickets to gauge individual reflections and lingering questions about TMS and BCI.



## Chapter 7: Lab introduction

In this series of lab exercises, you will explore the effects of different forms of brain stimulation through Python simulations. These labs are designed to provide practical experience in understanding how various stimulation techniques influence neural activity.

You will begin by simulating Transcranial Magnetic Stimulation (TMS) to understand its mechanisms and effects. In this lab, you will use Python to model the magnetic field distribution generated by a TMS coil and analyze the electric currents induced in cortical neurons. This exercise will help you grasp how TMS influences brain activity and its potential applications in neuroengineering and neuroscience research.

In the subsequent lab, you will simulate the effects of electrical stimulation on a neural network, creating a graphical user interface (GUI) for interactive experimentation. By adjusting different parameters and observing their impact on neural activity, you will gain insights into the dynamics of neural networks and the effects of various stimulation parameters. This hands-on approach will deepen your understanding of how electrical stimulation can modify neural responses and behavior.



# Chapter 7: Lab Example 1

## *Laboratory Exercise: Exploring TMS Mechanisms and Effects Using Python*



### **Objective**

This exercise aims to help students understand the mechanisms and effects of Transcranial Magnetic Stimulation (TMS) through simulation and analysis using Python. Students will simulate the magnetic field distribution generated by a TMS coil and analyze the induced electric currents in cortical neurons.

### **Materials Needed**

- Python programming environment (e.g., Jupyter Notebook)
- Python libraries: NumPy, Matplotlib, SciPy

### **Instructions**

#### **1. Setting Up the Environment:**

Install the necessary Python libraries if not already installed.

```
!pip install numpy matplotlib scipy
```

#### **2. Simulating the TMS Coil Magnetic Field:**

The following code simulates the magnetic field generated by a figure-eight TMS coil.

```
import numpy as np
import matplotlib.pyplot as plt
from scipy.constants import mu_0

def magnetic_field(x, y, coil_radius=0.05, current=1.0):
    """Magnetic field calculation for a figure-eight coil"""
    Bx = mu_0 * current * coil_radius**2 / (2 * ((x - coil_radius)**2 + y**2)**(3/2))
    By = mu_0 * current * coil_radius**2 / (2 * ((x + coil_radius)**2 + y**2)**(3/2))
```

```

    return Bx, By

    Create a grid of points
    x = np.linspace(-0.1, 0.1, 400)
    y = np.linspace(-0.1, 0.1, 400)
    X, Y = np.meshgrid(x, y)

    Calculate the magnetic field components
    Bx, By = magnetic_field(X, Y)

    Plot the magnetic field distribution
    plt.figure(figsize=(8, 6))
    plt.streamplot(X, Y, Bx, By, color=np.sqrt(Bx2 +
By2), linewidth=1.5)
    plt.title('Magnetic Field Distribution of TMS
Coil')
    plt.xlabel('x (meters)')
    plt.ylabel('y (meters)')
    plt.colorbar(label='Magnetic Field Strength
(Tesla)')
    plt.show()

```

### 3. Simulating Induced Electric Currents:

The induced electric currents in the cortical neurons can be simulated using the curl of the magnetic field.

```

def electric_field(Bx, By, dx):
    Calculate the electric field from the curl
    of the magnetic field
    Ex = np.gradient(By, dx, axis=1)
    Ey = -np.gradient(Bx, dx, axis=0)
    return Ex, Ey

    Calculate the electric field components
    dx = x[1] - x[0]
    Ex, Ey = electric_field(Bx, By, dx)

```

```

Plot the electric field distribution
plt.figure(figsize=(8, 6))
plt.streamplot(X, Y, Ex, Ey, color=np.sqrt(Ex2 +
Ey2), linewidth=1.5)
plt.title('Induced Electric Field Distribution')
plt.xlabel('x (meters)')
plt.ylabel('y (meters)')
plt.colorbar(label='Electric Field Strength
(V/m)')
plt.show()

```

#### 4. Analyzing the Results:

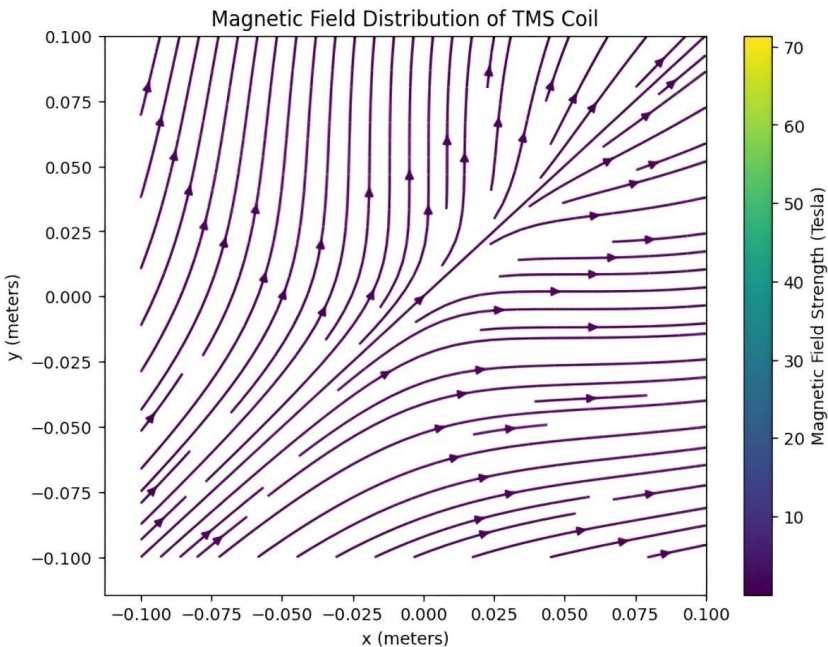


Figure 7.7: Laboratory Exercise Result 1: Magnetic Field Distribution

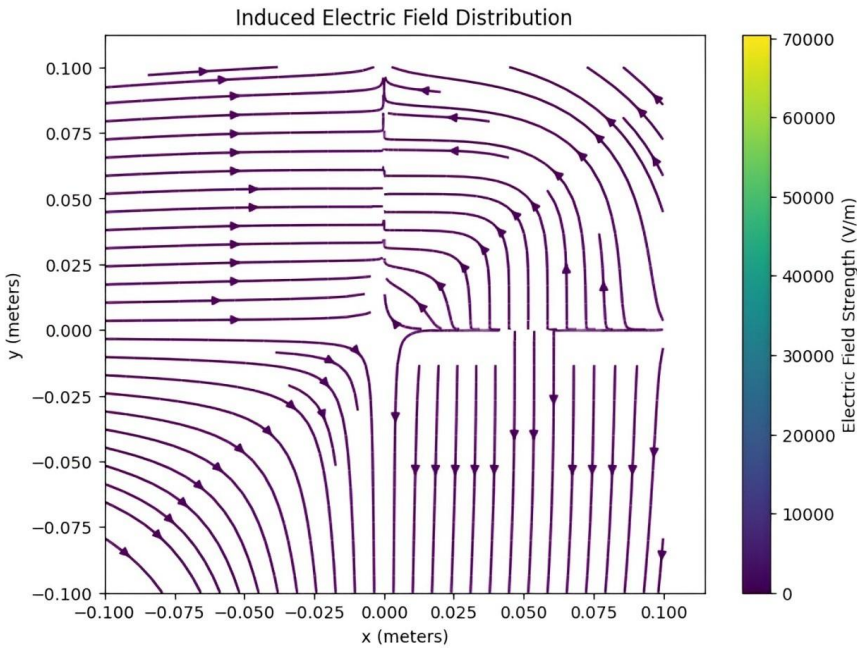


Figure 7.8 Laboratory Exercise Result 2: Electric Field Disbtribution

In this lab exercise, the simulation results are visualized in Figures 7.7 and 7.8, which depict the magnetic field distribution generated by a TMS coil and the corresponding induced electric field in cortical neurons. Figure 7.7 illustrates the magnetic field distribution, showing that the field is concentrated around the coil, with the strongest intensity near the center and gradually decreasing with distance. Figure 7.8 presents the induced electric field, which is derived from the curl of the magnetic field. The patterns in the electric field reflect the design of the coil, with the distribution playing a critical role in neuronal activation. The variations in the electric field's intensity and focality are key factors that can influence the effectiveness and outcomes of TMS therapy.

### ***Extension:***

For advanced students, modify the simulation to explore different coil configurations (e.g., circular coil, double cone coil) and their effects on the magnetic and electric field distributions. Additionally, it simulates the effects of varying stimulation parameters, such as frequency and intensity, on the induced electric fields.

By the end of this exercise, students should better understand the physical principles underlying TMS and how these principles translate into neuronal activation, contributing to the therapeutic effects observed in clinical settings.



# Chapter 7: Lab Example 2



## *Laboratory Exercise: Exploring Electrical Stimulation on Neural Networks Using Python*

### **Overview**

In this lab example, we will simulate the effects of electrical stimulation on a neural network using Python. We will create a graphical user interface (GUI) to allow for interactive experimentation with different parameters and observe how they affect neural activity. This hands-on approach will help students understand the dynamics of neural networks and the impact of various parameters on neural activity.

### **Goals of the Lab**

- Understand the basic structure and function of a neural network.
- Explore how electrical stimulation affects neural network activity.
- Learn how to create and interact with a GUI for scientific simulations.
- Analyze the impact of different parameters on neural network behavior, including the ratio of inhibitory neurons.

### **Requirements**

- Python (tested with 3.8 and later)
- Python libraries: NumPy, Matplotlib, Tkinter

### **Steps**

The first thing you need to do is go to the GitHub repository for this book. You can find it using this link:

[https://github.com/bddupre92/Neurobook\\_BME\\_UND](https://github.com/bddupre92/Neurobook_BME_UND)

After you have opened the GitHub, you need to navigate to Chapter 7, Lab Example 2. In this lab example, you will find the code for the simulation.

You will want to copy and paste the code into a script named `NNTest.py` and `NNGUI.py` into separate Script Files.

1. Setting Up the Environment
  - Install the necessary Python libraries if not already installed.
  - `!pip install numpy matplotlib tkinter`
2. Creating the Neural Network Simulation
  - Define functions to create the neural network, apply electrical stimulation, and simulate neural activity.
  - Implement a function to simulate neural activity considering both excitatory and inhibitory neurons.
3. Building the GUI
  - Create a graphical user interface using Tkinter that allows users to input parameters such as network size, stimulation intensity, number of steps, stimulation position, and the ratio of inhibitory neurons.
4. Running the Simulation
  - Users will input the desired parameters and simulate the GUI.
  - The simulation will display the initial and final neural network activity using heatmaps.

### ***Interpretation of Results***

- **Initial Neural Network Activity:** This shows the state of the neural network before stimulation, with only the neuron at the stimulation position activated.
- **Neural Network Activity After Stimulation:** Displays how the neural activity spreads from the initially stimulated neuron to its neighbors. The color intensity represents the activation level, with higher values indicating more activity.

### ***Key Observations***

- **Spread of Activation:** The stimulation spreads from the initially stimulated neuron to its neighbors, creating a pattern of activation influenced by the simulation parameters.
- **Effects of Inhibition:** Inhibitory neurons can significantly alter the activation pattern, demonstrating how inhibition can dampen neural activity and create more complex patterns.

## *Suggestions for Parameters to Modify*

1. Network Size:
  - **Impact:** Increasing the network size allows for observing how the spread of activation scales with larger networks.
  - **Output:** Larger networks may show more complex activation patterns and a broader activity spread.
2. Stimulation Intensity:
  - **Impact:** Higher intensity can result in stronger activation spread.
  - **Output:** Increased stimulation intensity can lead to more neurons being activated, resulting in a more widespread and intense pattern of activity.
3. Number of Steps:
  - **Impact:** More steps can provide insights into the longer-term effects of stimulation.
  - **Output:** Additional steps allow observing how the activation evolves, potentially showing sustained or diminishing activity.
4. Stimulation Position:
  - **Impact:** Changing the position can show the effect of stimulation at different network locations.
  - **Output:** Different stimulation positions can highlight how the network's structure and connectivity influence the spread of activation.
5. Inhibitory Neurons Ratio:
  - **Impact:** Varying the ratio of inhibitory neurons affects the network's balance between excitation and inhibition.
  - **Output:**
    - **Low Ratio (e.g., 0.01):** A low ratio of inhibitory neurons results in minimal inhibition, allowing for a broader and more intense activity spread, as shown in the first image.
    - **High Ratio (e.g., 0.2):** A higher ratio of inhibitory neurons introduces significant inhibition, reducing the overall activity and leading to a more localized and

subdued activation pattern, as demonstrated in the second image.

*Detailed Explanation of the Images*

*Image with Inhibitory Neurons Ratio at 0.01*

**Observation:** The neural network activity after stimulation shows a broad spread of activation.

**Interpretation:** With a low ratio of inhibitory neurons, the inhibition is minimal, allowing more neurons to become activated and maintain higher activity levels across the network.

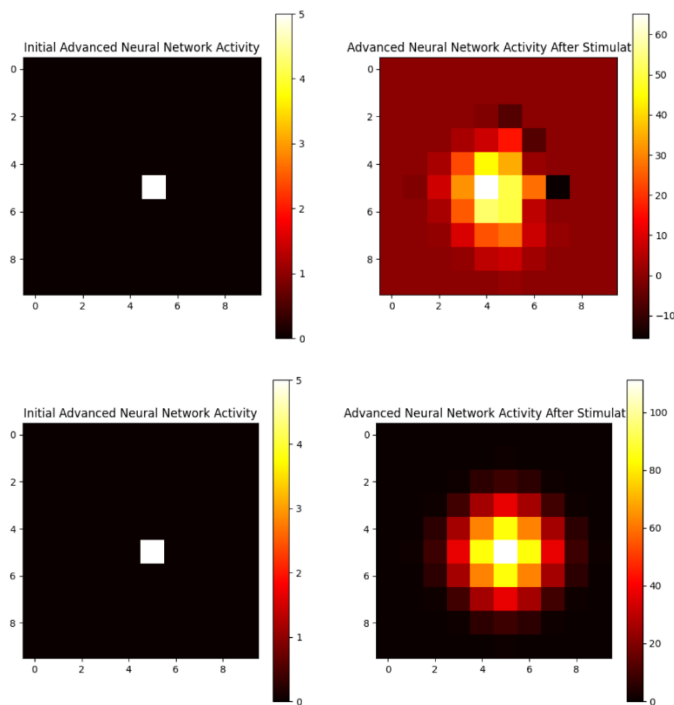


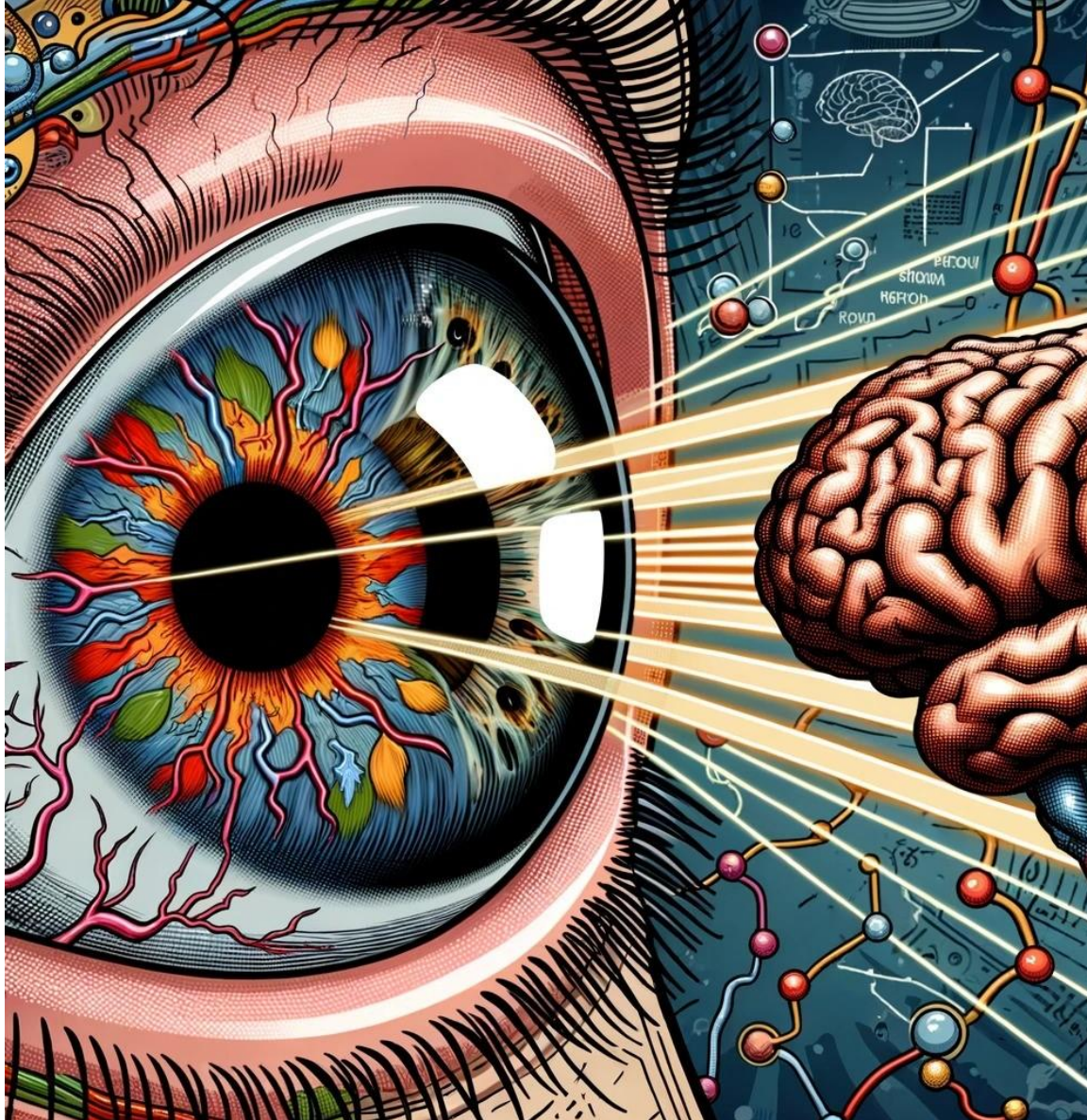
Figure 7.7: Neural Activity with Inhibitory Neurons

### ***Image with Inhibitory Neurons Ratio at 0.2***

- **Observation:** The neural network activity after stimulation is more localized, with reduced overall activity.
- **Interpretation:** A higher ratio of inhibitory neurons increases the inhibition, damping the spread of activation and resulting in fewer neurons being activated. The overall activity is more subdued and confined to a smaller region.

By adjusting these parameters, students can explore the intricate dynamics of neural networks and understand the delicate balance between excitation and inhibition. This hands-on lab provides valuable insights into the behavior of neural systems and the potential implications for neurostimulation therapies.





## Chapter 8

# Visual Voyage: Exploring the Wonders of the Visual System

# Introduction and Learning Objectives

So far, in your journey to discover neural engineering concepts, you have learned about the fundamental building blocks of the brain, ways to measure brain activity, and how to use that activity to impact society. Now, we will understand a captivating part of the nervous system: the visual system. The visual system is a network of structures working together to capture, process, and interpret light. In this chapter, we will go on another journey and discuss the anatomy of the visual system and how it works. This chapter will give you an overview of the visual system and its function. By the end of this chapter, you will be able to:

1. *Describe the anatomical features of the eye.*
2. *Explain the roles of the different parts of the visual system.*
3. *Understand the process of light interpretation and its importance in vision.*

## Anatomy of the Eye

### *The Layers of the Eye*

The human eye is a complex organ that is responsible for vision. The eye captures light stimuli from the environment and converts these into neural signals, which are then interpreted by the brain. The eye has three main layers: the outer, middle, and inner. The outer layer is made of the cornea and the sclera. The corneas are transparent structures that funnel light into the eye. The sclera is the white part of the eye, and its function is to provide protection and form to the eye. The middle layer included the choroid, ciliary body, and iris. The choroid contains blood vessels that supply the eye with much-needed nourishment. The ciliary body controls the shape of the lens, and the iris is a muscle that contracts and relaxes to control how much light is allowed to enter the eye by adjusting the size of the pupil. The lens, located behind the iris and pupil, focuses light onto the retina and is held in place by the suspensory ligament. The inner layer includes the retina, which contains several layers that

include photoreceptor cells, bipolar neurons, and ganglion cells. The layers of the retina function to detect light and convert it into electrical signals that are then sent to the brain through the optic nerve [178].

***The Chambers of the Eye***

The eye can also be divided into three main chambers. These chambers are filled with fluid to maintain the shape of the eye and provide nourishment. The

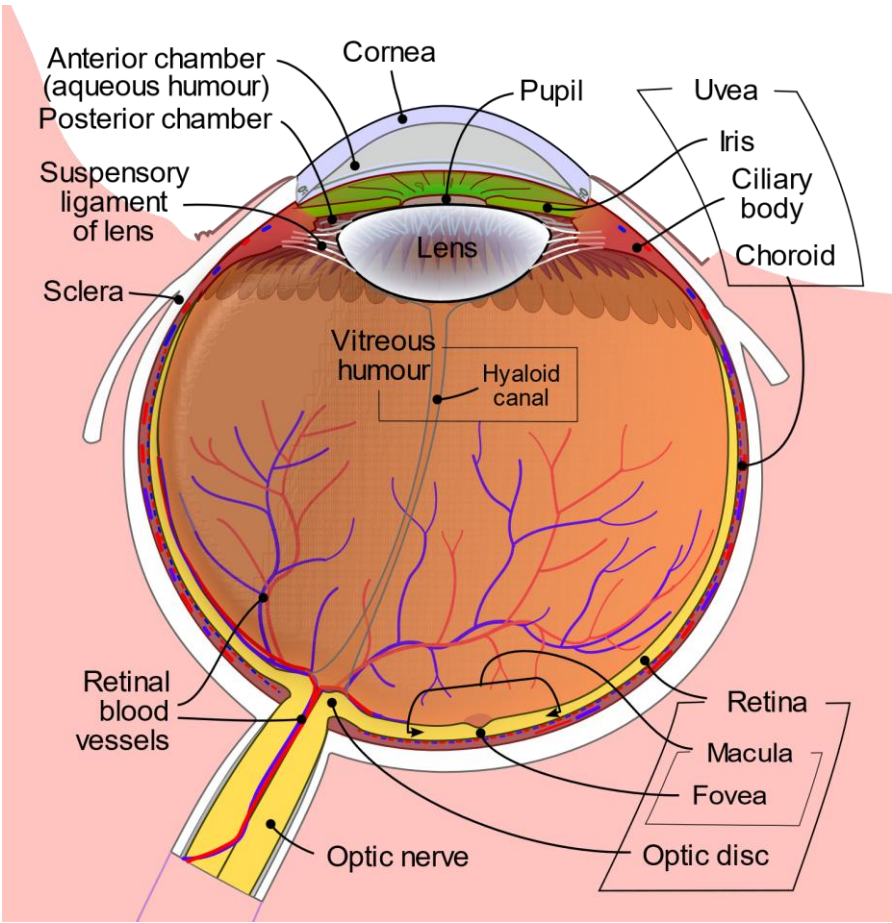


Figure 8.1: Anatomy of the Eye [180]

anterior chamber lies between the cornea and the iris and is filled with aqueous humor. Aqueous humor is a clear fluid that helps maintain intraocular pressure. The posterior chamber is between the iris and the lens and contains aqueous humor. This chamber plays a role in maintaining intraocular pressure and nutrient transport. The largest chamber is called the vitreous chamber and is behind the lens. This chamber is filled with vitreous humor, a gel-like substance that helps maintain the eye's shape. The hyaloid canal runs through this chamber from the lens to the optic disc to supply blood from the hyaloid artery to the lens. The macula is at the back of this chamber, and its center is called the fovea. The fovea is where eyesight is sharpest. [179]. See Fig. 8.1 [180] for a labeled graphic of the anatomy of the eye.

## **Light Refraction and Phototransduction**

Vision begins with light refraction as it enters the eye and ends when electrical signals are sent to the brain for image processing. This process ensures accurate interpretation of visual information, providing clear and detailed vision. The cornea and the lens play a critical role in refraction. The retina, equipped with photoreceptor cells (rods and cones), converts light into neural signaling through phototransduction.

### ***Refraction***

Refraction focuses on the light that enters the eye and hits the retina. When light passes through the chambers and different mediums, its speed changes, making it bend and refract. Refraction begins at the cornea, contributing to most of the eye's refractive power. Light reaches the lens after light passes through the cornea and aqueous humor. The lens provides fine adjustment to the focus of light through its ability to change shape, known as accommodation (Fig. 8.2 [181]). The ciliary muscle and suspensory ligaments flatten the lens for distant vision and round it for near vision. This control ensures the light converges accurately on the retina, making images clear and focused.

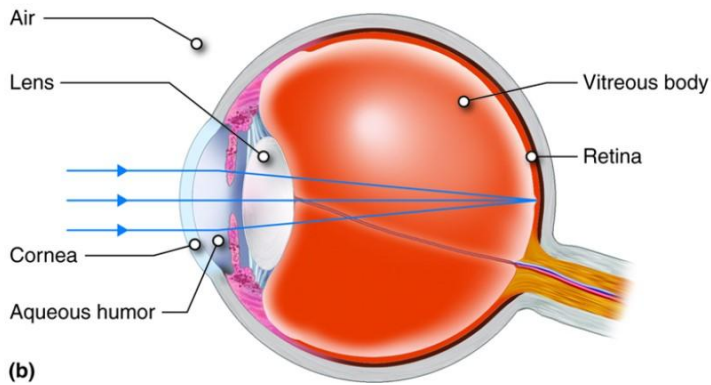


Figure 8.2: Refraction of Light in the Eye by the Lens [181]

### ***The Retina and its photoreceptors***

After light is channeled through these structures, the retina will convert the light into neural signals. The retina can do this through photoreceptor cells,

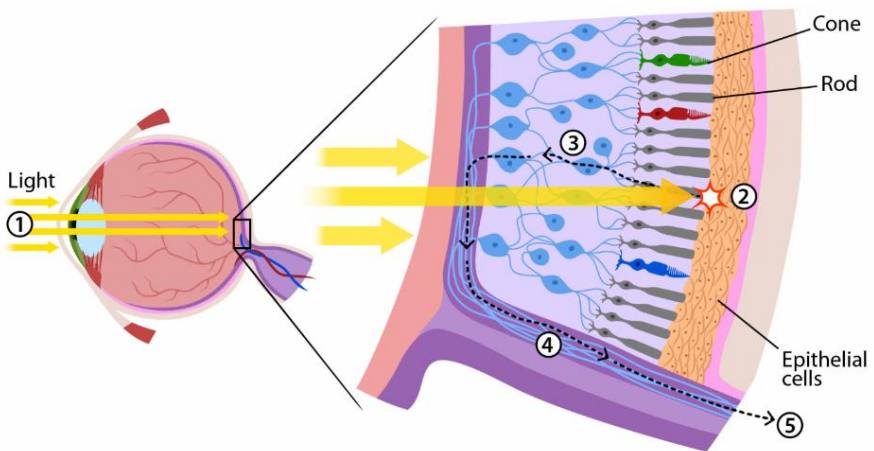


Figure 8.3: Retina layers responsible for phototransduction 1) light enters the eye and refracts on the retina 2) light passes to the outermost layer of the retina to the photoreceptors 3) bipolar cells mitigate and translate the signal to the ganglion cells 4) ganglion cells combine to make up the optic nerve 5) optic nerve sends the signal to the brain [182]

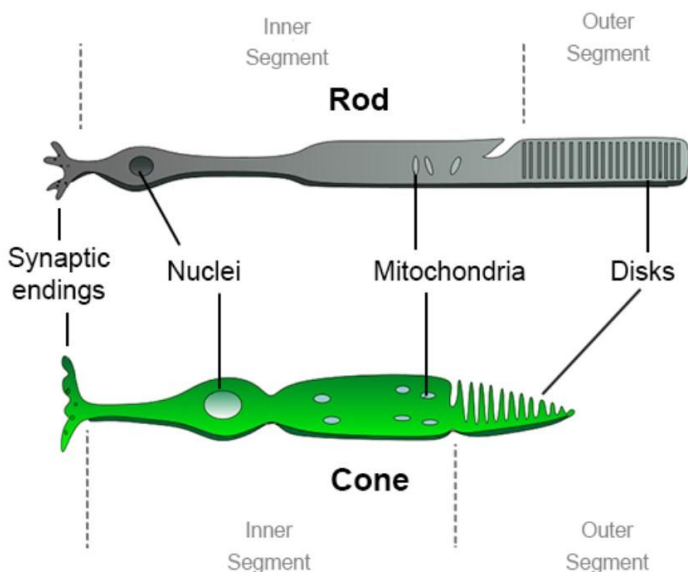


Figure 8.4: Diagram of a Rod and Cone [182]

rods, and cones (Fig. 8.3 [182]). The rods are highly light-sensitive and allow vision in low-light conditions. The rods cannot detect color and are concentrated around the retina's periphery. The cones are less light-sensitive but are responsible for color vision and visual acuity. The cones are concentrated in the fovea. As mentioned earlier, the retina also contains two other layers. The retina contains different cell types in these layers, such as bipolar and ganglion cells. These cells process visual information before transmitting it to the brain [183]. All the parts of the retina are crucial for phototransduction.

### ***Phototransduction***

Phototransduction begins when photopigments on the photoreceptors absorb light. This happens when light passes through the layers of the retina to reach the back layer that contains the photoreceptors. In rods, the photopigment is rhodopsin. The cones contain three photopigments corresponding to light wavelengths: red, green, and blue. When light activates these photopigments, it triggers a series of biochemical events that lead to hyperpolarization of the

photoreceptor membrane. The change in membrane potential causes the release of neurotransmitters (Chapter 1) that synapse with a bipolar cell. The bipolar cells modulate that signal and relay it to ganglion cells and the optic nerve. The optic nerve then carries this signal to the brain. This process ensures that light information is converted into neural signals the brain can interpret [6], [183]. Fig. 8.4 [182] shows a detailed image of light travels through the eye and into the layers of the retina to transform light stimuli into electrical signals to be sent to the brain.

## Visual Pathway

The visual pathway is a complex network that begins at the retina and extends to the visual cortex in the brain. In this section, we will explore the signals that signals take to the brain from the eye, the role of the visual cortex, and how

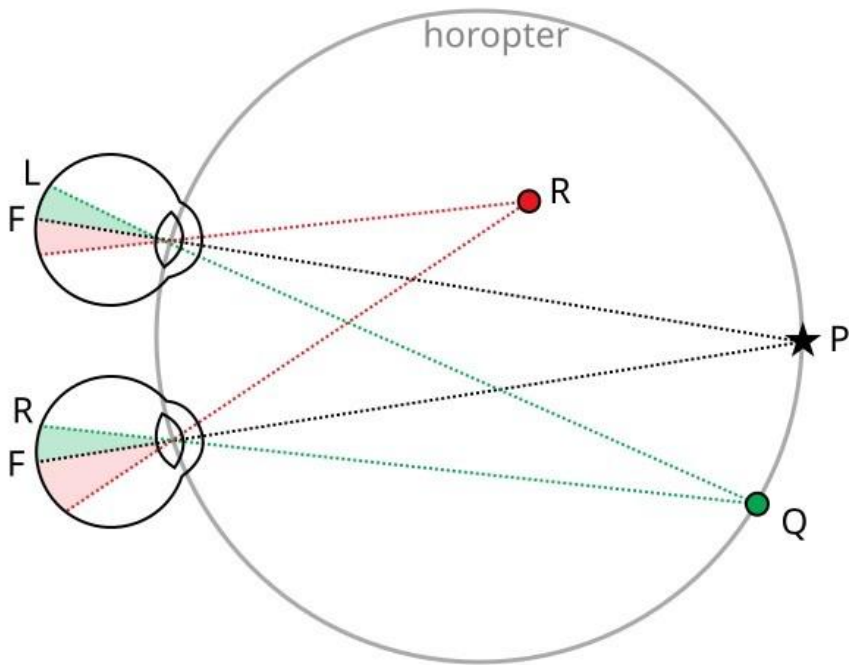


Figure 8.5: Binocular Vision [184]

this information is integrated and perceived to result in the visual experiences we encounter daily.

## ***The Journey to the Brain***

The visual information from the retina undergoes a journey to reach the visual cortex. After leaving the eye, the optic nerve travels through the optic chiasm, where the nerves partially cross—the nerve fibers stemming from each retina's nasal half cross to the brain's opposite side. The fibers from the temporal halves of the retina do not cross and remain on the same side. This crossing ensures that both hemispheres of the brain process visual information from each eye to create binocular vision and depth perception. Binocular vision is our ability to perceive a single, cohesive visual field from the input of both eyes, allowing for a three-dimensional understanding of our environment (Fig. 8.5 [184]). The overlapping fields of view from each eye provide the brain with slightly different perspectives, which are then integrated to create a single three-dimensional image.

After the optic chiasm, the visual information continues its journey along the optic tracts to the lateral geniculate nucleus (LGN) of the Thalamus. Recall from Chapter 1 that the thalamus is in the diencephalon and is the relay station for sensory signals to higher brain areas. The LGN refines and processes the visual signals before sending them to the primary visual cortex in the occipital lobe via optic radiation. The optic radiation is divided into two pathways. The upper path carries information from the lower visual field, and the lower pathway from the upper visual field [185].

## ***The Visual Cortex***

The primary visual cortex (V1) is the first cortical area to receive visual information from the LGN and is in the occipital lobe at the back of the brain. V1 is organized into a map of the visual field, called retinotopic organization. Retinotopic organization means neurons that pick up visual stimuli near each other in our visual fields also have neurons close together in the cortex. Fig. 8.6 [186] depicts the retinotopic organization of V. The retinotopic organization of V1 ensures that spatial relationships in the visual field are preserved during processing—V1 processes vision attributes, such as edges,

orientation, and motion. V1 functions as the initial decoder of the visual stimuli and then sends that information to be processed by other visual areas [6], [186].

The secondary visual areas (V2, V3, and V4) each specialize in processing different features of visual stimuli. For example, V2 processes complex shapes and textures, and V4 is crucial for color perception. These areas work together to integrate all the elements of visuals to build a more detailed and compressive representation of our visual field [6].

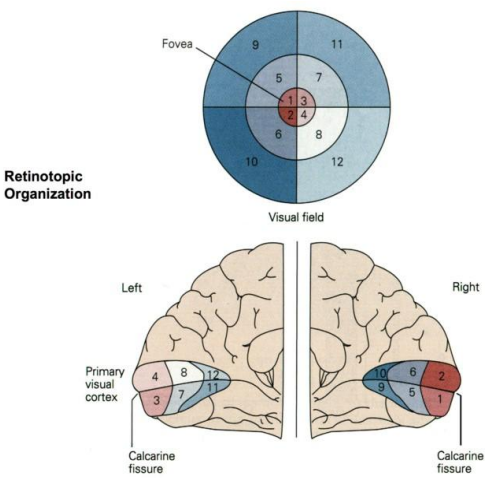


Figure 8.6: Retinotopic Organization of the Visual Cortex [186]

### ***Integration and Perception***

The integration and perception of visual information are complex processes that involve the coordination of multiple specialized regions within the brain. These processes are crucial for basic visual recognition and higher-level cognitive functions that enable us to navigate and interact with our environment effectively. The visual system is organized into two primary processing streams, each responsible for different aspects of visual perception.

#### ***The Dorsal Stream***

The Dorsal Stream originates in the occipital lobe, specifically the primary visual cortex (V1), and projects to the parietal lobe. This pathway is often called the "where" pathway because it is primarily involved in processing spatial information about the location and movement of objects in the visual field. The dorsal stream allows us to determine the position of objects relative to our own body, which is essential for spatial awareness. This spatial processing is critical for tasks such as reaching for an object, navigating through a room, or tracking

moving objects. In addition to spatial awareness, the dorsal stream plays a crucial role in movement coordination. It integrates visual information with motor commands to guide actions, such as adjusting the grip on a cup or timing a catch during a game. This stream is heavily involved in real-time processing, allowing for quick environmental adjustment.

### ***The Ventral Stream***

The Ventral Stream also begins in the occipital lobe but projects to the temporal lobe. It is known as the "what" pathway because it identifies and recognizes objects, faces, and scenes. The ventral stream is crucial for recognizing shapes, colors, and textures, which are the building blocks of object recognition. This pathway allows for identifying everyday objects, such as recognizing a car or distinguishing between different types of fruit. Certain areas, such as the fusiform face area (FFA), are specialized for recognizing faces within the ventral stream. This ability is vital for social interactions, allowing us to remember friends and family members and assess emotional expressions. The ventral stream also contributes to the recognition and interpretation of complex scenes, enabling us to understand the context of our surroundings, such as distinguishing a busy street from a quiet park.

Once visual information is processed through the dorsal and ventral streams, it is integrated with other sensory inputs and higher-order cognitive processes in various cortical regions. This integration is essential for creating a coherent and comprehensive visual perception. In higher cortical areas, visual information is combined with inputs from other sensory modalities, such as auditory, tactile, and proprioceptive signals. This multisensory integration allows for a more robust and accurate perception of the environment. For instance, hearing a car while seeing its approach helps to gauge its speed and distance more effectively than visual input alone. The brain uses context and prior knowledge to interpret visual information. This involves integrating visual data with memories, expectations, and experiences stored in the brain. For example, recognizing a familiar face in a crowd or identifying an object based on its surroundings relies on this contextual processing. Attention plays a critical role in visual perception by selecting which visual information is processed more deeply and which is filtered out. Higher cortical areas, such as the

prefrontal cortex, interact with visual areas to direct attention to relevant stimuli, such as focusing on a pedestrian while driving or finding a friend in a crowded room. Integrated visual information is also used to guide actions. For example, the brain's ability to recognize a door handle and coordinate the movement to grasp and turn it seamlessly involves the interaction of visual perception and motor planning areas. The parietal lobe plays a key role in this visuomotor integration through its connection with the dorsal stream.

The brain's ability to integrate and interpret visual information rapidly and accurately is essential for interacting with our environment. This capability is needed for nearly every aspect of daily life, from simple tasks like reaching for a cup of coffee to complex activities like playing sports or driving a car. The speed and accuracy of visual processing are critical for survival, allowing for quick reactions to potential threats or opportunities in the environment. For example, detecting a moving vehicle in peripheral vision and responding appropriately directly results from the brain's efficient visual integration. Visual integration is also fundamental to learning and memory. By associating visual cues with experiences, the brain builds a repository of knowledge that informs future behavior. This process is crucial for tasks ranging from recognizing familiar objects to navigating new environments. In social contexts, the ability to quickly recognize faces, interpret expressions and understand gestures relies on the seamless integration of visual information. This capacity enables effective communication and helps us navigate complex social dynamics.

The integration and perception of visual information in the brain involves a sophisticated network of pathways and cortical regions working together. The dorsal and ventral streams process visual stimuli, such as spatial location and object identification, which are then integrated with other sensory inputs and cognitive processes in higher cortical areas. This complex integration allows us to coherently understand our surroundings and interact with the world in meaningful and adaptive ways. The efficiency and accuracy of this system are essential for everything from basic survival to complex social interactions, highlighting the remarkable capabilities of the human brain.

# Visual Disorders and Disease

Now that we have explored how the visual system works, addressing visual disorders and diseases is essential. Visual disorders can significantly impact an individual's quality of life, ranging from minor vision impairments to complete blindness. Understanding these conditions is necessary for accurate diagnosis and for innovating new treatments. Advancements in neuroengineering offer promising solutions and help enhance our ability to manage and treat these disorders. The following section will discuss some of the most common visual disorders and diseases and the current geoeengineering solutions for their treatment and management.

## *Refractive Errors*

Refractive errors occur when the eye's shape (optical imperfections) prevents light from focusing directly on the retina, causing blurred vision. These refractive errors include nearsightedness or myopia, farsightedness or hyperopia, astigmatism, and presbyopia. These conditions are caused by structural irregularities in the eye, including the eyeball's length or the cornea's shape. Common symptoms of refractive errors include difficulty seeing distant or close objects. Treatments for refractive errors include advanced engineering solutions such as wavefront-guided LASIK and intraocular lenses (IOLs). These technologies use eye measurements to customize treatments to improve visual outcomes. Additionally, adaptive optics are being adapted for retinal imaging and corrective procedures to provide vision correction [187].

## *Cataracts*

Cataracts are characterized by lens clouding, leading to decreased vision and even blindness. Risk factors for cataracts include age, diabetes, smoking, and prolonged exposure to ultraviolet light. Symptoms include blurry vision, glare, and difficulty seeing at night. The primary treatment for cataracts is surgical removal of the clouded lens and replacement with IOLs. Another engineered cataract treatment is femtosecond laser-assisted cataract surgery (FLACS), which allows for more precise and less invasive surgical procedures.

Additionally, advanced bioengineering lenses can improve patient visual outcomes and treatment safety and efficacy [188].

### ***Glaucoma***

Glaucoma involves damage to the optic nerve, usually due to high intraocular pressure, leading to progressive vision loss. Factors that contribute to glaucoma include age, genetic disposition, and certain medical conditions. Early stages of glaucoma typically are asymptomatic, but advanced stages can cause peripheral vision loss. Engineering advancements have led to the development of minimally invasive glaucoma surgeries. These surgeries reduce the intraocular pressure in the eye. Additionally, devices like micro stents and shunts can improve eye fluid drainage. Continuous intraocular pressure monitoring systems that use intelligent contact lenses can also provide real-time data to help manage and treat the disease [189].

### ***Macular Degeneration***

Macular degeneration is the deterioration of the macula, leading to loss of central vision. Age-related macular degeneration (AMD) is influenced by age, genetic factors, and lifestyle choices. Symptoms include blurred central vision and difficulties in recognizing faces. Cutting-edge treatments include retinal implants and gene therapy. Retinal implants, or bionic eyes, can partially restore vision by converting light into electrical signals that stimulate the remaining retinal cells. Gene therapies aim to correct genetic defects that cause AMD. Additionally, imaging technologies like optical coherence tomography (OCT) provide detailed retina images, aiding in early disease detection and monitoring [190].

### ***Diabetic Retinopathy***

Diabetic Retinopathy is a complication of diabetes that affects the blood vessels of the retina and leads to vision impairment. High blood sugar levels can damage the retinal blood vessels, causing them to swell or lose entirely. This can lead to vision problems. Symptoms include floaters, blurred vision, and dark areas of vision. Technologies to treat this condition include laser photocoagulation to seal leaking blood vessels to prevent further damage.

Vitrectomy, removing the vitreous gel and replacing it with oil, can help clear the blood from the eye and repair retinal detachment. Like glaucoma, engineered continuous glucose monitoring systems and insulin pumps can help maintain optimal blood sugar levels, reducing the risk of this disease.

### ***Retinal Detachment***

Retinal detachment happens when the retina separates from the underlying tissue, which can lead to vision loss if it is not treated. Causes for retinal detachment include trauma, severe myopia, and age-related changes. Symptoms include sudden flashes of light and a shadow over the field of vision. Advances in surgical techniques and instruments have improved the success of retinal detachment repairs (Fig. 8.7 [191]). Additionally, developments in retinal imaging and microsurgery tools have enhanced the precision and outcomes of these surgical procedures [192],[193].

### ***Strabismus***

Strabismus, or cross eyes, is a condition where the eyes do not correctly align when looking at an object. This misalignment can result in double vision or the brain ignoring inputs from one eye to void confusion, leading to amblyopia or lazy eye. Causes can include muscle imbalances, nerve damage, or

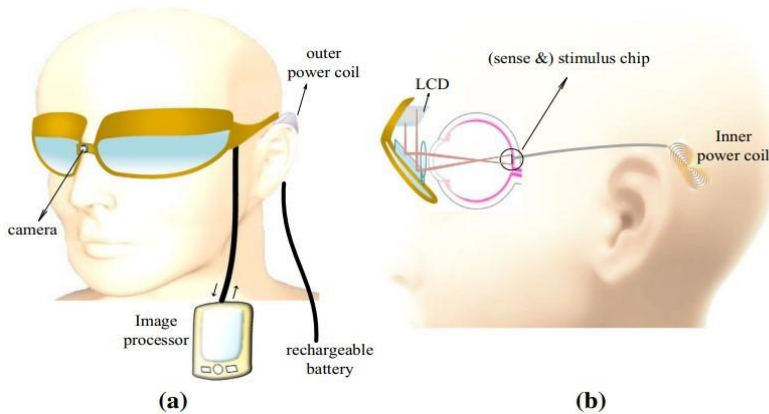


Figure 8.7: Image of typical retinal implants with (a) outer and (b) inner components [191]

congenital issues. Symptoms include misaligned eyes, difficulty with depth perception, and double vision. Robotic-assisted surgeries are being developed to improve the accuracy and outcomes of surgeries used to fix the alignment of the eyes. Vision therapies using virtual reality (VR) and computer-based exercises have also been used to strengthen the eye muscles to improve coordination. These engineering technologies offer new ways to treat and manage this condition [194].

Understanding these disorders and diseases is crucial for improving treatment and management strategies. These conditions range from common refractive errors to more severe issues like glaucoma, which can significantly impact individuals' quality of life. Integrating neuroengineering solutions into ophthalmology has enabled more effective treatments and better management of visual disorders. From laser-assisted surgeries to retinal implants, the field of vision care is evolving. As we move forward, continued research and development in neuroengineering and ophthalmology will be essential in addressing the challenges posed by visual disorders.

## **Chapter 8: Summary**

This chapter explored the visual system's intricate world, anatomy, function, and various disorders affecting vision. We began with a detailed examination of the eye anatomy. We discussed the essential structures and their role in capturing and processing light and understanding how light stimulus goes through the eye. We then explored the visual pathway and how visual information travels from the retina to the brain. The discussion of retinotopic organization within the visual cortex shows the precision with which our brain processes visual stimuli. We then discuss various visual disorders, including their causes, symptoms, and current treatments, along with innovative neuroengineering solutions in the field of ophthalmology. You are encouraged to continue your knowledge and investment in and support for research and development in neuroengineering and ophthalmology. By fostering collaboration and investing in cutting-edge technologies, we can advance our understanding and treatment of visual disorders. In the next few chapters, we

will explore neural engineering technologies that harness vision, diving deeper into how these innovations are being developed and applied.



## Chapter 8: Learning activities

### Learning Activity 8.1

***Game: let us make a trivial pursuit game.  
Create ten cards with four topics: anatomy,  
functionality, math, and graphs.***



#### ***Objective***

Students will create a section of a Trivial Pursuit game, designing question cards covering anatomy, functionality, math, and graphs related to neuroengineering.

#### ***Materials***

- Index cards or paper
- Pens or markers
- Internet access (for research)
- Reference materials (textbooks, notes)

#### ***Time***

30-45 minutes

#### ***Instructions***

##### ***Introduction (5 minutes):***

1. Introduce the activity and explain its goal: to create a section of a Trivial Pursuit game focused on neuroengineering topics.
2. Divide the class into small groups of 3-4 students.

##### ***Card Creation (25-30 minutes):***

3. Instruct each group to create 10 Trivial Pursuit cards, with questions and answers, covering the following topics:
  - Anatomy (e.g., brain regions, neural structures)
  - Functionality (e.g., how different parts of the brain work, neurochemical processes)

- Math (e.g., calculations related to neuroengineering, statistical methods)
- Graphs (e.g., interpreting data from neuroimaging, EEG/MEG results)

***Guidelines for Creating Cards:***

- Each card should have a question on one side and the answer on the other.
- Questions should vary in difficulty.
- Ensure accuracy by referencing reliable sources.
- Use a mix of question types (e.g., multiple choice, true/false, short answer).

***Group Sharing (5-10 minutes):***

4. Have each group share a few of their most interesting or challenging questions with the class.

***Conclusion (5 minutes):***

5. Collect the cards and explain that they will be used in a future Trivial Pursuit game session to review and reinforce learning.
6. Summarize the activity, emphasizing the importance of reviewing key concepts engagingly and interactively.

## **Learning Activity 8.2**

### ***Role-Play Game - Parts of the Eye***

#### ***Objective***

Students will learn and reinforce their knowledge of the anatomy and functions of different parts of the eye through an interactive role-play game.



## ***Materials***

- List of eye parts (e.g., cornea, lens, retina, optic nerve, iris, pupil, sclera, vitreous humor, etc.)
- Slips of paper with the names of different eye parts
- A timer
- Crown or small prize for the champion

## ***Time***

20-30 minutes

## ***Instructions***

### ***Introduction (3 minutes):***

1. Introduce the activity and explain its goal: to reinforce knowledge of the anatomy and functions of the eye through a fun and interactive role-play game.
2. Explain the rules of the game and how it will be played.

### ***Preparation (2 minutes):***

3. Randomly assign each student a part of the eye by drawing slips of paper with the names of different eye parts.
4. Give students 2 minutes to prepare by reviewing their assigned part's anatomy and function.

### ***Role-Play and Questioning (15-20 minutes):***

5. Begin the rounds of questioning. One student starts by answering questions from their peers about their assigned eye part.
6. If students answer correctly, they continue to the next round. They are eliminated if they answer incorrectly or if another student correctly guesses their part.
7. Continue the rounds until only one student remains. This student is the champion.

### ***Conclusion and Crowning the Champion (5 minutes):***

8. Crown the last student standing as the champion with a small prize or a crown.

9. Summarize the key points learned during the activity and emphasize the importance of understanding eye anatomy and function.

---

## Learning Activity 8.3

### *Concept Map - Parts of the Visual System*

#### *Objective*

Students will create a concept map of the visual system to organize and understand its components and functions visually. This activity will involve individual work, peer, and group sharing to enhance collaborative learning.



#### *Materials:*

- Large sheets of paper or poster boards
- Markers or colored pens
- Internet access or textbooks (for reference)
- Sticky notes (optional)

#### *Time:*

30-45 minutes

#### *Instructions:*

##### *Introduction (5 minutes):*

1. Introduce the activity and explain its goal: to create a concept map that organizes and illustrates the components and functions of the visual system.
2. Briefly explain what a concept map is and provide an example if necessary.

***Individual Task (10 minutes):***

3. Ask each student to create a concept map of the visual system. They should include key components such as the cornea, lens, retina, optic nerve, and other relevant parts and show how they are connected.
4. Allow students to use reference materials like textbooks or online resources to help them.

***Peer Share (5 minutes):***

5. Once the individual maps are complete, pair up the students.
6. Instruct each pair to share their concept maps, discuss the similarities and differences in their maps, and provide feedback.

***Group Share (10 minutes):***

7. Form small groups of 4-5 students and have each pair join another pair.
8. In these groups, students will share their concept maps again, integrating the best elements from each map to create a comprehensive group concept map.
9. Provide large sheets of paper or poster boards and markers for the groups to draw their combined concept maps.

***Class Presentation (10-15 minutes):***

10. Each group will present their combined concept map to the class, explaining the components and their connections.
11. Facilitate a class discussion to compare the different maps and highlight key points.

***Conclusion (5 minutes):***

12. Summarize the key points learned during the activity, emphasizing the importance of understanding the visual system's components and their interconnections.
13. Encourage students to reflect on how creating and sharing concept maps helped them understand the visual system better.



## Chapter 8: Lab introduction

In this series of lab exercises, you will explore advanced techniques for visual system analysis using MATLAB. These labs generate interactive visualizations and utilize specialized toolboxes to model various aspects of eye anatomy and function.

You will begin by creating an interactive eye anatomy image using MATLAB. This lab will guide you through generating and manipulating a detailed visualization of the eye, enhancing your understanding of its structure and functions. Ensure that MATLAB is installed on your system; if not, refer to the installation instructions provided in Chapter 1: Lab Example 1.

In the subsequent lab, you will work with the Image System Engineering Toolbox for Biology (ISETBio), a MATLAB toolbox designed for in-depth visual system analysis. ISETBio enables you to create spectral radiance scenes and model their effects on various components of the human visual system, including eye optics, movements, cone absorptions, and retinal cell properties. You will download and install ISETBio from the provided GitHub link and apply its features to explore complex visual system simulations. By the end of these labs, you will gain hands-on experience in visualizing eye anatomy and utilizing advanced tools for modeling visual processes.



# Chapter 8: Lab Example 1



## *Overview*

We will generate an interactive eye anatomy image using MATLAB in this lab. You should already have MATLAB installed; however, if you don't, there are instructions on downloading it in Chapter 1: Lab Example 1.

## *Requirements*

- MATLAB
- Texture images of the iris, sclera, and retina

## *Steps*

First, go onto the internet and find three images: one of the iris, one of the retina, and one of the sclera. Make sure that these images are saved as .jpg files. For this lab to work correctly, you must know each anatomical component and save the right pictures. If you need a refresher on these anatomical components, refer to section 9.2 of this chapter.

After you have MATLAB open, start a new script and go to the GitHub repository at this link:

[https://github.com/bddupre92/Neurobook\\_BME\\_UND](https://github.com/bddupre92/Neurobook_BME_UND)

Navigate Chapter 8 code 1 and open it in MATLAB.

## *Script Structure*

### *Generate Unit Sphere*

- Create a unit sphere to serve as the base for the eye model.

### *Prepare Figure*

- Configure the figure properties such as color, axis, and grid.

### *Main Globe (Sclera)*

- Define the radius and generate the surface for the main globe representing the sclera.

### ***Iris Sphere***

- Define the radius and generate the surface for the iris.
- Adjust coordinates to position the iris on the globe properly.

### ***Read Images***

- Load the texture images for the iris, sclera, and retina.

### ***Texture Mapping***

- Apply the texture images to the corresponding surfaces.
- Optionally mirror the images to enhance the definition.

### ***Rotate and View Adjustment***

- Rotate the main globe for correct orientation.
- Adjust the view to display the front of the eye and part of the back.

### ***Interactive Features***

- Enable interactive manipulation of the view with rotate3d.

### ***Retina Texture***

- Add a textured surface to represent the retina at the back of the eye.

## ***Key Functions Used***

### ***sphere***

- **Usage:** `[x, y, z] = sphere();`
- **Purpose:** Generates the coordinates for a unit sphere.

### ***surf***

- **Usage:** `mainGlobe = surf(xm, ym, zm, 'EdgeColor', 'none', 'FaceAlpha', 0.5);`
- **Purpose:** Creates a 3D surface plot.

### ***imread***

- **Usage:** `imgIris = imread(irisImagePath);`
- **Purpose:** Reads an image file into MATLAB.

### ***set***

- **Usage:** `set(mainGlobe, 'FaceColor', 'Texturemap', 'CData', CDglobe, 'FaceAlpha', 0.5);`

- **Purpose:** Sets properties for graphics objects.

#### *rotate*

- **Usage:** rotate(mainGlobe, [1 0 0], -90);
- **Purpose:** Rotates the graphics object.

#### *view*

1. **Usage:** view([-1, -1, 0.5]);
2. **Purpose:** Sets the viewpoint for the 3D plot.

#### *camorbit*

- **Usage:** camorbit(0,0,'camera');
- **Purpose:** Orbits the camera around the scene.

#### *rotate3d*

- **Usage:** rotate3d on;
- **Purpose:** Enables interactive 3D rotation of the plot.

### ***Further considerations***

See lines 22, 23, and 24 under

```
% Define the paths to the images.
```

You must make a path to your photos from your computer and paste them here. To create a path to an image, right-click it and select “Copy as Path.” You will then paste that into the MATLAB code. Make sure you have ‘’ around the file path name. You must ensure your images are saved in your MATLAB drive, where you create the path. If you do not have a MATLAB drive, follow this link to set it up.

<https://www.mathworks.com/products/matlab-drive.html>

Once you have entered your file paths, click run. You should see a figure window (Fig. 8.8) with your eyeball inside!

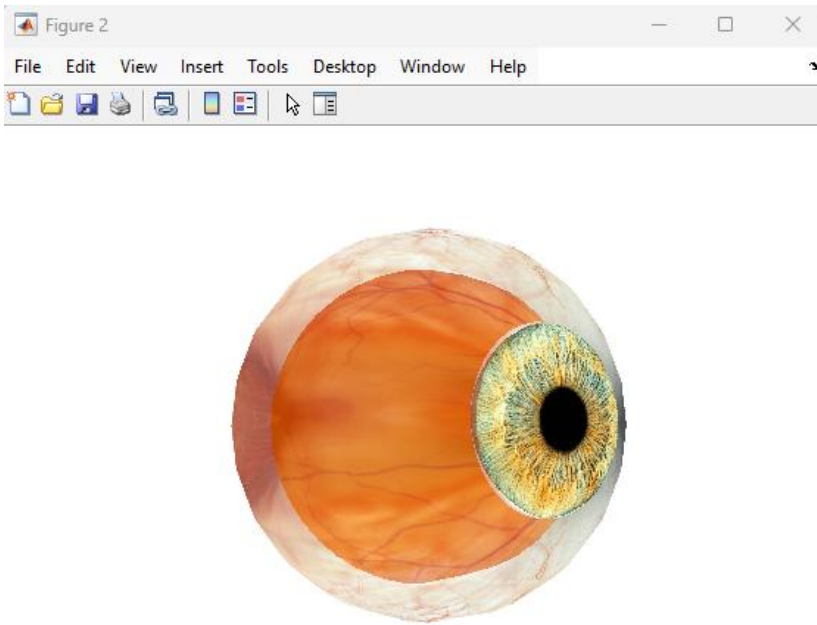


Figure 8.8: Code One Results

We will take this further and look at it with different eyes.

Open a new script on MATLAB and get back to GitHub. Navigate to Chapter 8, code 2, and open it in MATLAB.

## ***Description of Differences in Structures and Key Functions***

This updated MATLAB script builds upon the previous one by generating and visualizing two 3D eyeballs with different iris textures. Here are the key differences and additions:

## ***Key Additions and Changes***

### ***Multiple Image Paths***

The script now includes an additional path for a second iris texture image:

```
irisImagePath2 = 'iris image 2 path'; % Path to the iris  
texture image for the second eyeball
```

### ***File Existence Checks***

The script checks if all specified image files exist, including the second iris image:

```
if ~isfile(irisImagePath)
    error('Iris image file not found: %s', irisImagePath);
end
```

### ***Reading Images***

The script reads the second iris image in addition to the other images:

```
try
    imgIris = imread(irisImagePath);
catch ME
    error('Error reading iris image: %s', ME.message);
end
```

### ***Generating Two Eyeballs***

Coordinates and surfaces for the second eyeball are generated with a horizontal shift to separate them visually:

```
% Define the coordinates for the second eyeball
x_shift = 12; % Adjust as needed
xm2 = xm + x_shift;
xi2 = xi + x_shift;
```

### ***Surface Generation and Texture Mapping for the Second Eyeball:***

The script creates the main globe, iris, and retina surfaces for the second eyeball:

```
% Generate the surface for the second eyeball
mainGlobe2 = surf(xm2, ym, zm, 'EdgeColor', 'none',
    'FaceAlpha', 0.5);
irisGlobe2 = surf(xi2, yi, zi, 'EdgeColor', 'none');

% Apply mapping for the second eyeball with a different iris
image
```

```

set(mainGlobe2, 'FaceColor', 'Texturemap', 'CData', CDglobe,
'FaceAlpha', 0.5);
set(irisGlobe2, 'FaceColor', 'Texturemap', 'CData', imgIris2,
'EdgeColor', 'none');

% Texture mapping for the second eyeball
rotate(mainGlobe2, [1 0 0], -90);

% Add retina texture to the back of the second eye
retina2 = surf(xr + x_shift, yr, -zr, 'FaceColor',
'Texturemap', 'CData', imgRetina, 'EdgeColor', 'none');

```

## ***Summary of Key Functions***

### ***isfile***

- **Usage:** `if ~isfile(irisImagePath2)`
- **Purpose:** Checks if a file exists at the specified path. Used to ensure all image files are available before proceeding.

### ***imread***

- **Usage:** `imgIris2 = imread(irisImagePath2);`
- **Purpose:** Reads an image file into MATLAB. Extended to include reading the second iris image.

### ***surf***

- **Usage:** `mainGlobe2 = surf(xm2, ym, zm, 'EdgeColor', 'none', 'FaceAlpha', 0.5);`
- **Purpose:** Creates a 3D surface plot. Used to generate the main globe, iris, and retina surfaces for both eyeballs.

### ***set***

- **Usage:** `set(mainGlobe2, 'FaceColor', 'Texturemap', 'CData', CDglobe, 'FaceAlpha', 0.5);`
- **Purpose:** Sets properties for graphics objects. Used to apply textures to the surfaces of both eyeballs.

### ***rotate***

- **Usage:** `rotate(mainGlobe2, [1 0 0], -90);`

- **Purpose:** Rotates the graphics object. Used to orient both eyeballs correctly.

Use the following images (Fig. 8.9) for `irisImagePath` and `irisImagePath2`. Save them to your MATLAB drive, make an image path, and copy and paste them into the code. Do not forget to copy and paste your image paths for the sclera and the retina.

Now, run your code. You should have a figure box with two eyes in it. If you receive an error code that states 'XX image file not found,' you have not created the image path correctly and saved it into your MATLAB drive.

Can you tell me what is off with these two eyes? The right pupil is much smaller than the right eye pupil. Do you know what this is called? You may know about this disorder if you have taken a neuroanatomy class before. Hint: we did not discuss it in this chapter. This is called Horner's syndrome. Horner's syndrome is a rare neurological syndrome that results from underlying nerve damage from a stroke, tumor, or spinal cord injury. Symptoms of this syndrome include smaller pupils (miosis), drooping eyelids (ptosis), and little to no sweating on the affected side of the face (anhidrosis). To treat this syndrome, some individuals will need the removal of a tumor or appropriate medical treatments.

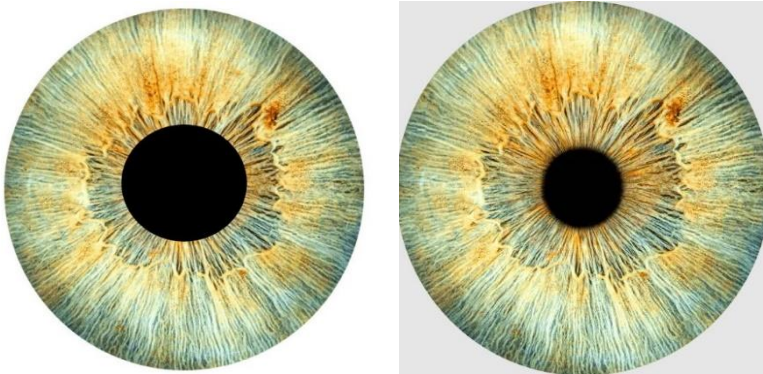


Figure 8.9: Images for Code Two



## Chapter 8: Lab Example 2

### *Overview*

In this lab example, we will utilize the Image System Engineering Toolbox for Biology, or ISETBio for short.

ISETBio is a set of tools for MATLAB that can conduct visual system analysis by providing capabilities to create spectral radiance scenes and model their effects on human optics, eye movements, cone absorptions, retinal cell properties, and more. The link to download and install ISETBio from their GitHub can be found here:

[GitHub - isetbio/isetbio: Tools for modeling image systems engineering in the human visual system front end.](https://github.com/isetbio/isetbio)

You can learn more about ISETBio from Cottaris et al. [195].

As part of this lab, we will reinforce our understanding of the visual system anatomy by creating a plot of cone density in the eye. This will be accomplished by utilizing a tutorial script from the ISETBio toolbox in MATLAB.

### *Requirements*

- MATLAB
- ISETCam
- ISETBio

### *Description*

As we learned in the visual system chapter, cones are concentrated in the fovea. The cones are responsible for our color vision but are less light-sensitive than rods. For this reason, our anatomical knowledge is cleverly applied during times of darkness. This concentration of cones in the center of our vision creates a centrally focused blind spot at night. Instead of looking directly at an object when it is dark, you can look 5-10 degrees away from the center of gaze and have better light sensitivity, effectively enhancing your night vision. Let's look at a plot of the cone density to illustrate this concept effectively.



Within MATLAB, the path to the ISETBio tutorial/cones folder. We can find a “t\_conesDensity.m” script file in this folder. If you open this, the ISETBio team has succinctly described the script's function and the data's source. They use two resources to obtain the cone density estimates Curcio et al. [170] and Song et al.[171].

The script file is short and to the point. A quick evaluation of the script will show you how the ISETBio toolbox works to obtain the final goal of plotting cone density. The “pos” portion of the code specifies the location of some object outward from the fovea in millimeters. The “ang” portion defines the angle of view around the eye in radians. This allows us to plot a full range of the eye map (Fig. 8.10). Then, the distribution of cones from the two research papers above is defined.

Run the script for t\_conesDensity.m and evaluate the final logarithmic scale plot that is produced:

**Summary**

We utilized the ISETBio toolbox in MATLAB to run a basic tutorial that allowed us to visualize the concentration of cones across the retina. This

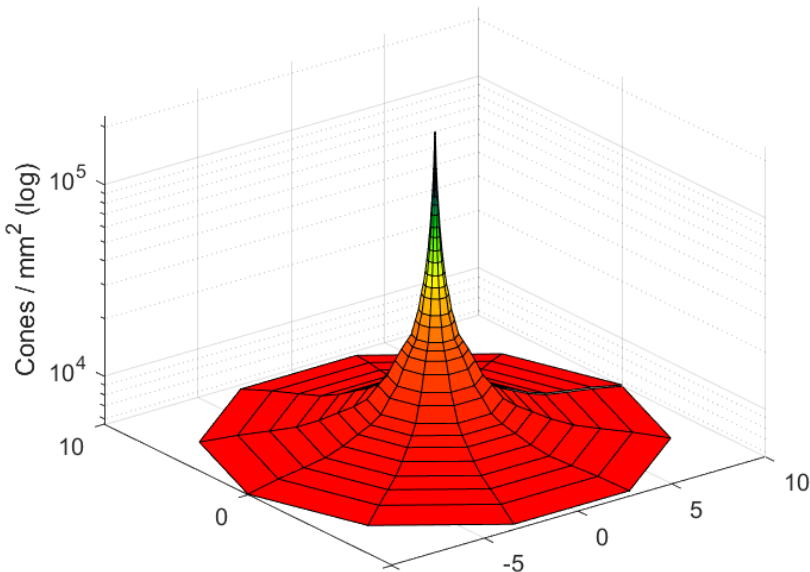


Figure 8.10: Concentration of Cones across the Retina

provides us with a basic understanding of how the ISETBio toolbox functions and may guide you in thinking of creative ways to employ this toolbox for your own research goals.





## **Chapter 9**

# **The Eyes Have it: Unlocking Secrets with Eye Trackers**

# Introduction and Learning Objectives

Eye tracking is a unique and essential tool with many uses in neuroengineering applications. Eye tracking generically refers to measuring gaze, where someone is looking, or the motion of an eye. It enables a researcher to investigate various visual and cognitive functions. Additionally, it pairs well with other neuroengineering techniques to provide robust and detailed data. The basic principle of eye tracking involves utilizing hardware to detect and record eye movements. This approach can allow researchers such as yourself to analyze how the eyes interact with visual stimuli. Eye tracking objectively measures where and how long an individual looks at specific locations or objects. This can be used to guide engineering designs or assist in neuropathology diagnosis.

This chapter will explore various applications of eye tracking in engineering. By the end of this chapter, you'll be able to understand the following concepts:

1. *Understand the anatomical and engineering principles of eye-tracking technology.*
2. *Identify basic hardware components of eye trackers.*
3. *Describe various applications of eye-tracking experimentation across multiple fields.*

## Review of Anatomy Applied to Eye Tracking

Building on our previous chapter's in-depth review of visual system anatomy, let's explore some important eye-tracking specifics. The primary structures in eye tracking include the cornea, lens, retina, iris, pupil, and optic nerve.

### ***Cornea***

The transparent front layer collects incoming light and directs it to the retina.

### ***Lens***

It is located behind the cornea and fine-tunes the focus of light onto the retina.

### ***Retina***

A layer of photoreceptor cells at the back of the eye detects light and converts it into electrical signals sent to the brain.

### ***Pupil***

The dark opening of the eye that is formed by the iris.

### ***Iris***

The colored part of the eye controls the size of the pupil and the amount of light entering the eye.

### ***Optic Nerve***

Transmits visual information from the retina to the brain for processing.

Understanding the basic anatomical structures and their functions helps understand how eye tracking works, designing experiments, and interpreting results. For instance, changes in pupil size can indicate variations in emotional state, while abnormalities in eye movement patterns can signal neurological issues.

## **Eye Tracking Technology**

### ***Basics of Eye Movement***

You should know a few unique eye movements that can be important when understanding eye tracking, formulating experiments, or interpreting eye-tracking data.

### ***Saccades***

These are rapid eye movements that orient the gaze toward something. These movements are notable for tasks such as reading, where the eyes jump from word to word.

### ***Nystagmus***

The involuntary, rhythmic movement of the eyes, often in response to neurological conditions. Nystagmus can occur in the horizontal, vertical, or rotational plane. This movement type is commonly associated with impairment and can indicate vestibular dysfunction.

### ***Fixations***

Fixation occurs when the eyes are stationary, allowing for detailed visual processing.

### ***Smooth Pursuit***

These are slower, controlled eye movements that track moving objects. Smooth pursuits are crucial for sports and driving, where continuous tracking of moving objects is necessary. Lack of smooth pursuit is another common vestibular dysfunction indicator.

Understanding these different eye movements is vital for eye-tracking research as they provide insights into the underlying neural mechanisms of visual processing.

### ***Types of Eye Trackers***

Eye trackers can be classified into three categories based on their design and application: remote, head-mounted, and integrated systems. Examples of these devices are shown in Fig 9.1 [198]. Each type has distinct advantages and limitations that make them suitable for specific research and practical applications.

Remote eye trackers are portable, consumer-level devices that track eye movements from a distance. They are typically mounted on a table or



Figure 9.1: Types of eye trackers [198]

integrated into laptops or webcams, making them convenient for various settings in controlled environments or comfortable living spaces. However, their accuracy can be lower than that of more specialized systems due to limitations in camera quality or excessive motion.

Table-mounted eye trackers are differentiated from “remote-eye trackers” by being research-grade hardware. These trackers are also placed on a desk or table to face the participant. They use high-resolution cameras and commonly infrared light to capture detailed images of the eyes. Table-mounted eye trackers offer higher accuracy and precision than remote systems and are more often used in controlled laboratory environments for more controlled research. Head-mounted eye trackers are worn on the participant’s head as standalone devices or integrated into glasses, helmets, or other headsets. These systems offer greater mobility and the ability to track eye movements in real-world settings with higher quality and accuracy than remote systems. Glasses-based trackers are lightweight devices with small cameras that track the wearer’s eye movements, suitable for studies involving driving, sports, and more.

Integrated eye trackers are becoming more widespread in virtual reality (VR)

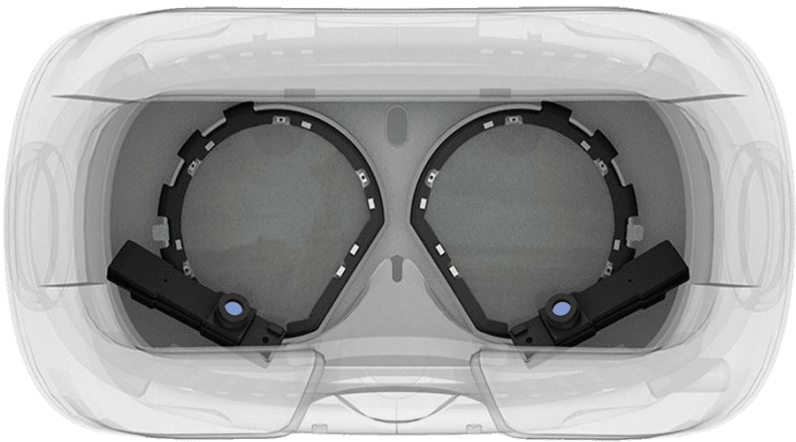


Figure 9.2: Integrated eye trackers for VR systems [199]

or augmented reality (AR) headsets like Fig. 9.2 [199]. VR/AR headsets with

eye tracking open new research avenues, including studying responses to simulated environments or placing subjects into otherwise difficult or unsafe real-life settings. The potential for studying human responses in various atmospheres presents unique implications for future research.

Eye tracking is also increasingly integrated into automotive systems and consumer electronics, such as cars and smartphones. Each type of eye tracker has its advantages and disadvantages, which will be discussed later.

## ***Hardware Components***

Modern eye trackers are sophisticated devices that rely on advanced hardware components to measure and analyze eye movements with high precision. These components include high-resolution cameras, infrared light sources, and various supporting technologies that capture detailed and accurate data on where and how users look.

### ***High-Resolution Cameras***

The core of any eye-tracking system is its high-resolution camera, which captures detailed eye images, particularly focusing on the pupil and corneal reflections. The resolution of these cameras is critical as it determines the clarity and precision with which the eye's movements are recorded. Modern eye trackers typically operate at high frame rates, often around 1000Hz (1000 frames per second). This high frame rate is essential for accurately tracking rapid eye movements, such as saccades, which are quick, simultaneous movements of both eyes in the same direction. Capturing these movements requires a fast camera and the ability to process a large amount of data in real-time.

High-resolution cameras ensure that even the smallest eye movements, such as micro-saccades, are detected. This spatial accuracy is vital for applications requiring precise eye movement data, such as psychology, neuroscience, and human-computer interaction research.

### ***Infrared Light Sources***

Infrared light sources are used to illuminate the eye, specifically the pupil, to enhance contrast and improve the accuracy of eye-tracking measurements. Infrared light creates a distinct reflection from the cornea, known as the corneal reflection or "glint," which is used with pupil detection to determine the gaze

direction. One significant advantage of infrared light is that it is invisible to the human eye, meaning it does not interfere with the user's natural vision or tasks. This allows the eye tracker to operate without distracting the user or altering their behavior, which is crucial for maintaining the integrity of the data collected. Infrared illumination reduces the impact of ambient lighting conditions, which can vary significantly between different environments. Whether the user is in a brightly lit room or a dimly lit space, the infrared light ensures consistent eye-tracking performance by providing uniform eye illumination. This consistency is particularly important in applications like usability testing or driver monitoring, where lighting conditions may be unpredictable. Eye trackers with infrared light are significantly more accurate than those without. The enhanced contrast provided by infrared illumination allows for more precise detection of the pupil and corneal reflections, leading to better tracking of gaze direction and eye movements. This increased accuracy is critical in applications where even minor errors can lead to significant misinterpretations, such as in cognitive research or medical diagnostics. Without infrared illumination, eye trackers are more susceptible to errors caused by changes in ambient light, reflections, or shadows on the face. These factors can distort the eye's image and lead to inaccurate measurements. Infrared light mitigates these issues by providing a consistent lighting source, reducing the likelihood of tracking errors, and improving the overall reliability of the data. Infrared-enhanced eye trackers offer better usability in a wider range of conditions. They are less dependent on the external environment, making them suitable for various settings, from controlled laboratory environments to more dynamic real-world scenarios. This flexibility is essential for expanding eye-tracking technology in virtual reality, where lighting conditions vary dramatically.

Integrating high-resolution cameras and infrared light sources in modern eye-trackers represents a significant advancement in eye-tracking technology. These components work together to provide accurate, reliable, and consistent tracking of eye movements, even in challenging conditions. The benefits of infrared-enhanced eye trackers, including increased accuracy, reduced errors, and enhanced usability, make them indispensable tools across various applications, from cognitive research and human-computer interaction to virtual

reality and medical diagnostics. As eye-tracking technology continues to evolve, the role of these core hardware components will remain critical in enabling new and innovative uses of eye-tracking data.

## ***Software for Eye Tracking***

Eye-tracking software is responsible for collecting and processing data from the hardware. This is where the pupillary detection and gaze direction are truly handled. The software uses sophisticated algorithms to calculate the gaze direction and record the data for further analysis. The software can also manage artifacts such as unintentional motion or detect blinking.

Modern eye-tracking systems offer real-time data acquisition and can provide immediate feedback on eye movements. This real-time capability is essential for applications such as user interface design, where immediate adjustments based on eye movement data can enhance usability and performance.

## ***Algorithms and Mathematical Models***

Various algorithms and math models are applied to detect and track the pupil, gaze correctly, or blink. Different algorithms can be used to accomplish different goals. Some common methods include circular Hough transform, I-VT, stereo geometry, convolution neural network, or other machine learning approaches.

### ***Pupil Detection***

Many algorithms have been developed to detect the pupil itself. A commonly discussed algorithm for this application is the circular Hough transform, although there are many more [200], [201]. The detection of the pupil and measurement of pupil velocity can be used to distinguish fixations, saccades, smooth pursuit, or other eye movements we previously discussed[202].

### ***Gaze Mapping***

Gaze mapping is a very common application of eye-tracking models. This involves translating eye movement data into meaningful information, like determining where a subject is looking on a screen and for how long [203], [204]. This process requires calibration, where the eye tracker is adjusted to each individual's eyes to ensure accurate mapping of gaze points. This can

produce “heat maps” showing concentrations of fixation and patterns of focus to determine how subjects typically interpret something. This can have a variety of applications, such as designing a research poster, a movie poster, an advertisement, or many other applications. There are many approaches to utilizing or analyzing eye-tracker data. Gaze mapping is just one common and easily applicable approach.

### ***Corneal Reflection***

An interesting aspect of gaze mapping is called corneal reflection. This involves utilizing the reflection of the infrared light source on the cornea, called a glint, to determine gaze direction. This approach analyzed the position of the corneal reflection to the pupil’s center to calculate an accurate gaze direction.

This is not an all-encompassing overview, and it is important to appreciate new advancements occurring with the application of deep-learning artificial intelligence technologies to perform even more accurate eye-tracking analysis. These AI techniques can harness large datasets and information from previous models to perform even more precise and robust analyses within eye-tracking systems.

## ***Experimental Design***

Setting up an eye-tracking experiment involves several steps that may vary depending on the technology you are employing and the environment within which you are using it.

### ***Calibration***

Each participant must undergo a calibration process where they are asked to look at known points on a screen. This process adjusts the eye tracker for individual eye anatomy and movement pattern differences.

### ***Lighting Conditions***

Optimal lighting is crucial for accurate eye tracking, especially when using lower-quality hardware. While infrared illumination helps mitigate the impact of ambient light, the experimental setup should avoid direct light sources that can create reflections and interfere with tracking. In dark environments, using

green or red light can provide illumination without interfering with night-vision sensitivity or other responses.

### ***Participant Instructions***

Subjects should be given clear instructions to ensure they understand the tasks and the importance of maintaining a stable head position during tracking.

## **Performance and Limitations**

### ***Accuracy and Precision***

Accuracy within the realm of eye trackers refers to the degree to which the measured gaze corresponds to the actual point of fixation. Precision, on the other hand, refers to the consistency and repeatability of the measurements. High accuracy and precision are critical for detailed analysis of eye movements. Factors affecting accuracy and precision have already been touched on, including the hardware's quality, the software's effectiveness, and the experimental setup.

### ***Pupil Size and Eye Shape***

Variations in pupil size and eye shape can impact the accuracy of eye tracking. For example, larger pupils can be easier for the eye tracker to detect, improving accuracy. However, changes in pupil size due to lighting conditions or cognitive load can introduce variability. Additionally, iris color can play a role in pupil size and response. Individuals with lighter-colored eyes may have more constricted pupil size in certain lighting conditions than dark eyes in the same environment. The degree of iris constriction or dilation can also vary from person to person and affect measurements.

### ***Glasses and Contacts***

Eyewear can create reflections and distortions, making eye tracking difficult depending on the hardware selection. Advanced algorithms may compensate for this without issue, and hardware selection, such as wearable eye-trackers, may negate this issue if coupled with prescription lenses.

# **Applications in Research**

## ***Cognition***

Eye tracking can provide insights into cognitive processes by revealing how attention is allocated and prioritized. For example, eye movements can indicate how individuals process information and how long they process it while reading, solving problems, or making decisions. This can be paired with other experimental techniques, such as the fMRI, to provide several layers of analysis that can be interpreted in tandem.

## ***Human Factors***

The human factor is a meaningful topic in many different fields. In the automotive field, for example, human factors research may be concerned with innumerable safety questions:

1. How and when people respond to signage while driving.
2. Driver behavior during emergencies.
3. Driver behavior in novel roadway designs.
4. How intoxication alters driver response times.

This is just a short list outlining the potential applications of eye-tracking research in ways that can benefit society. Additional fields include aviation, gaming, and even the film industry.

## ***Psychology***

In psychology, eye tracking can be used to study emotion, social, or developmental processes. For example, researchers can investigate how autistic individuals process social cues by analyzing their eye movements when viewing faces. Eye tracking can also be used to study attention biases in anxiety and depression by examining how individuals respond to emotional stimuli.

# **Available Products on the Market**

Several common eye-tracking products have unique features and capabilities that range from consumer to research-grade. When selecting an eye-tracking system, it is important to consider the advantages and disadvantages of each

product to determine the best fit for your research or application. With that said, the first step is identifying your experimental design and, thus, your research environment. The major criterion in this regard is the level of portability, as this is the major limitation of the device you select. The major products available today are discussed, but the list is not exhaustive.

### *Tobii*

Tobii is a well-known company that produces eye-tracking products and is best known for its glasses-based system [8]. Their glasses contain several cameras and infrared light sources and utilize corneal reflection, pupil, and stereo geometry to perform accurate eye tracking and analysis. They also have screen-based eye trackers that can be used in various applications, making them a versatile option for consumer and research purposes.

The Tobii products are user-friendly and are offered at a range of applications from consumer-level to research-grade. The glasses-based systems are particularly valuable for naturalistic studies, as they allow for real-world eye tracking with minimal intrusiveness. Naturally, with this level of portability, battery life becomes a potential disadvantage. Additionally, it is specified that data should be sampled up to 100 Hz, which could be a disadvantage depending on the sampling level your research requires.

### *SR-Research*

Another well-researched eye-tracking product is the EyeLink system by SR Research. The EyeLink products are head-mounted or table-mounted, as shown in Fig. 9.3 [205]. These devices provide high resolution and accuracy and utilize pupil detection and corneal reflection methods, making them suitable for highly detailed studies, such as those in cognitive neuroscience or psychophysics.

The SR-Research EyeLink is well known for its high accuracy and resolution. As such, their system is reported to have a 2000 Hz sampling rate and 0.15-degree accuracy. The disadvantage comes both at cost and complexity levels. Additionally, it may not be suitable for naturalistic studies like the Tobii.

## *iMotions*

iMotions has several eye trackers, including screen-based, glass, VR, and webcam-based systems [206]. Their systems harness various algorithms and models, allowing for eye-tracking applications that best suit your experimental design. This flexibility makes iMotions a strong choice for researchers wanting customizable solutions for multiple contexts. The flexibility of their eye-tracking offerings is a clear advantage for researchers. The cost of these systems may provide limitations for certain budgets.

## *Pupil Labs*

Pupil Labs is another company with various eye tracker systems similar to iMotions [207]. Their eye-tracking systems harness diverse algorithms and configurations that support various research needs. Pupil Labs also places a strong emphasis on open-source solutions, which is called Pupil Core. This can be extremely advantageous for researchers who value open-source alternatives and cost-effective solutions. This enables high versatility that can be adapted to various experimental designs. Although some consider the open-source nature an advantage, others consider this a disadvantage, and it is up to each



Figure 9.3: SR-Research table mounted eye tracker from SR-Research [205]

user to make that decision. The primary limitation of this could be the support and resources provided.

These different products can help you accomplish unique research goals in various environments. This allows a researcher to develop novel designs and applications that can help answer specific research questions.

## **Emerging Trends in Eye Tracking Tech**

A discussion on emerging trends for any technology in 2024 is incomplete without including artificial intelligence (AI). Recent advancements in the AI space, along with machine learning, have begun to enhance current eye-tracking technology. A Google search of the topic will further solidify this statement. First, AI can be harnessed to improve the speed and precision of eye-tracking technology. This can be in the form of improved detection algorithms or improved sensitivity to eye movements.

Additionally, AI could be used to detect and classify eye movements and predict eye movements. This idea is already being implemented in “Neuromarketing” methodologies. This idea will be further discussed in the section on ethical considerations.

In the medical space, AI-enhanced technology can improve medical diagnostics through the previously discussed techniques. Due to the increased sensitivity and accuracy, early-stage detection of neurological disorders may become a reality. Given the fairly low-cost implementation of eye trackers relative to other medical technology, this can provide broader consumer-level treatment.

Although this chapter briefly touched on VR and AR, it is still a “new” and growing field. The growing incorporation of eye tracking in these systems will surely open new avenues for research in neuroengineering. As VR/AR and AI technology further integrate, one can foresee incredibly realistic immersive environments for neurological simulation studies that will produce more realistic results.

Another trend in eye technology, and by extension eye-tracking, is its application to biometrics. Currently, cellphones utilize “face” or fingerprint

recognition. The use of eye biometrics is a foreseeable application. Some police departments are already using eye biometrics for identification purposes.

## **Challenges and Future Directions**

### ***Accuracy and Precision of Eye Trackers***

The level of accuracy and precision is always a considerable factor when a researcher implements certain technologies. Eye-trackers' goals within the research space will always be high accuracy and precision. The previous discussion on AI and machine learning in space opens an avenue for achieving this goal. For those interested in implementing eye-trackers in neuroengineering, the tremendous growth in this technology will provide several opportunities for novel research ideas.

Additionally, using IR may not fully address the challenge of collecting eye-tracking data in low-light conditions. Additional approaches may be developed to address some of the challenges faced during low-light conditions.

### ***Ethical Considerations and Privacy***

There are ethical considerations and data privacy concerns with integrating eye-tracking technology into everyday technology. Personalized iris data, eye movement data, and, by extension, medical can reveal sensitive information about an individual. There will be a need for clear guidelines and regulations that follow current human subject testing guidelines on collecting and storing personal data. This also means researchers applying this technology must prioritize transparency and consent to prevent misuse of this information. Additionally, with eye-tracking technology being potentially used for biometrics, the public should be confident in the accuracy and privacy considerations that are being considered.

### ***Multimodal Integration in Neuroengineering Research***

As we have covered in this chapter, eye tracking is uniquely powerful in its portability and affordability. The multimodal integration of eye-tracking with other methods, such as fMRI, fNIRS, or EEG, could provide a more

comprehensive understanding of cognitive and emotional processes. This again presents unique research ideas and challenges for the future.

## Chapter 9: Summary

Eye tracking technology is unique, affordable, accessible, and has applications in any scientific field. The portability and application in naturalistic environments provide the option to develop any number of unique studies that have the potential to benefit society. Technological advancements, especially with VR headsets and AI, promise even more applications in future research. Whether your interests lie in psychology, medicine, or engineering, there is room for eye-tracking research in each field.

In the next journey of this book, you will explore the worlds of psychophysics and virtual reality. This does not mark the end of your discussion of eye-trackers. It highlights just how applicable eye-tracking technology is across various domains. For those of you with a special interest in eye-tracking research, the multimodal integration possibilities within the psychophysics space will undoubtedly pique your interest.



## Chapter 9: Learning activities

### Learning Activity 9.1

#### *Learning Activity: Drawing a Functional Block Diagram (FBD) of an Eyetracker*



#### *Objective:*

Students will understand the components and functionality of an eye-tracker by creating a functional block diagram (FBD) and discussing their designs with peers.

#### *Materials Needed:*

- Paper
- Pens/Pencils
- Markers (optional)
- Reference materials on eye trackers (e.g., textbooks, articles, diagrams)

#### *Activity Outline:*

1. **Introduction (10 minutes)**
  - Briefly introduce the concept of eye trackers and their applications in various fields, such as psychology, marketing, and UX/UI design.
  - Explain what a Functional Block Diagram (FBD) is and its importance in illustrating the components and workings of a system.
2. **Individual Work (20 minutes)**
  - Each student will individually draw an FBD of an eye-tracker. They should include and label the main components, such as the camera, infrared light source, processing unit, and software interface. They should also show the data flow from the eye movement to the final output on the computer screen.

- Encourage students to consider the interactions between different parts and the system's workflow.
- 3. **Pair Share (15 minutes)**
  - Students will pair up with a classmate to share and discuss their FBDs. Each pair should compare their diagrams, discuss the differences and similarities, and provide constructive feedback to each other.
  - Pairs should refine their diagrams based on the discussion, ensuring all essential components and data flows are included.
- 4. **Class Discussion and Reporting (15 minutes)**
  - Each pair will present their refined FBDs to the class. They should explain the components they included and the rationale behind their design.
  - After each presentation, allow time for questions and comments from the class. This will help identify any common misconceptions and clarify any doubts.
- 5. **Conclusion (5 minutes)**
  - Summarize the key points discussed during the class presentations.
  - Highlight any particularly well-done diagrams and explain why they stood out.
  - Encourage students to continue exploring how different systems are designed and function by creating FBDs for other devices.

### ***Assessment:***

- **Participation:** Ensure that each student actively participates in the individual work, pair share, and class discussion.
  - **Accuracy and Completeness:** Evaluate each student's FBD for accuracy and completeness, ensuring all main components are included and correctly labeled.
  - **Collaboration:** Assess how well students work in pairs and contribute to the class discussion. Learning activity 9.2
-

## Learning Activity 9.2

### *Evaluating an Eyetracker Game*

#### *Objective*

Students will gain hands-on experience with an eye-tracker through an interactive game and evaluate its effectiveness and functionality by working collaboratively.

#### *Materials Needed*

- Computers or tablets with internet access
- Access to the eye-tracker game at [GazeRecorder](#)
- Paper and pens/pencils for note-taking

#### *Activity Outline*

1. Introduction (10 minutes)
  - Introduce the concept of eye trackers and their applications in various fields.
  - Explain the purpose of the activity: to explore and evaluate an eye-tracker game.
2. Individual Game Play (20 minutes)
  - Each student will individually access the eye-tracker game on [GazeRecorder](#).
  - They will spend time playing the game, paying close attention to how the eye-tracker responds to their eye movements, the accuracy, and the user interface.
  - Students should take notes on their experiences, focusing on the game's functionality, usability, and any issues encountered.
3. Pair Share (15 minutes)
  - Students will pair up with a classmate to discuss their experiences with the game.
  - In pairs, students should compare notes and discuss the following:
    - How accurately did the eye-tracker follow their eye movements?



- Any challenges or difficulties they faced while playing the game.
  - Suggestions for improvements or features they found particularly useful.
4. Class Discussion and Reporting (15 minutes)
    - Each pair will present their findings to the class.
    - Presentations should cover the main points of their discussion, highlighting both positive aspects and areas for improvement.
    - Encourage other students to ask questions and add their observations.
  5. Conclusion (5 minutes)
    - Summarize the key points discussed during the class presentations.
    - Highlight common themes or unique insights from the evaluations.
    - Discuss the potential applications of eye-tracker technology in various fields and how such games can be used for research or training.

## ***Assessment***

- **Participation:** Ensure that each student actively participates in the individual gameplay, pair share, and class discussion.
  - **Quality of Evaluation:** Evaluate each pair's presentation for thoroughness, clarity, and insightfulness.
  - **Collaboration:** Assess how well students work in pairs and contribute to the class discussion. Learning activity 9.3
-

## Learning Activity 9.3

### *Creating and Analyzing Heat Maps with an Eyetracker*



#### ***Objective***

Students will learn how to create heat maps using an eye-tracker app based on their webcams, understand the calibration process, and discuss their experiences and findings with the class.

#### ***Materials Needed***

- Computers with internet access and webcams
- Access to an eye-tracker app that can generate heat maps (e.g., GazeRecorder, WebGazer.js)
- Paper and pens/pencils for note-taking

#### ***Activity Outline***

1. Introduction (10 minutes)
  - Briefly introduce eye-tracking technology and its applications, focusing on how heat maps can provide insights into user behavior and preferences.
  - Explain the purpose of the activity: to create a heat map of their favorite webpage and understand the calibration process.
2. Individual Activity (30 minutes)
  - Selecting a Webpage:
    - Each student will choose their favorite webpage to analyze (e.g., a news site, social media page, or any frequently visited website).
  - Calibration:
    - Before creating the heat map, students need to calibrate the eye tracker app. Explain the importance of calibration: it ensures the eye-tracker can accurately detect where the user is looking on the screen.

- Students should follow the app's instructions to complete the calibration sequence, which typically involves looking at specific points on the screen.
- **Creating the Heat Map:**
  - After calibration, students will navigate their chosen webpage while the eye-tracker records their eye movements.
  - The app will generate a heat map based on where they frequently look on the page.
- **Note-Taking:**
  - Students should take notes on the following:
    - Their experience with the calibration process: Was it easy or difficult? Why is calibration necessary?
    - Observations about the generated heat map: Which areas of the webpage attracted the most attention? Were there any surprises?
    - Thoughts on the overall experience and potential improvements.
- **Class Discussion and Reporting (20 minutes)**
  - Each student will present their findings to the class, addressing the questions about the calibration sequence and their heat map observations.
  - Encourage students to compare their heat maps and discuss common patterns or differences.
  - Facilitate a discussion on the importance of calibration and how it affects the accuracy of the eye-tracker.
- **Conclusion (5 minutes)**
  - Summarize key points from the class discussion, highlighting common insights and unique observations.
  - Discuss the broader implications of eye tracking technology and heat maps in understanding user behavior and improving webpage design.



## Chapter 9: Lab introduction

In this series of lab exercises, you will explore eye-tracking and the simulation of eye movements using MATLAB. These labs are designed to provide hands-on experience with image processing and dynamic system modeling, deepening your understanding of visual tracking and eye movement dynamics.

You will run a simplistic eye-tracking exercise in the first lab using MATLAB. The focus will be on implementing the Hough transform and Viola-Jones algorithms. The Viola-Jones algorithm detects and classifies faces, noses, eyes, mouths, and the upper body in images, giving you practical experience in facial feature detection and classification.

In the second lab, you will create MATLAB code to generate simulated saccades, which are rapid, ballistic eye movements as they shift focus from one point to another. Using a second-order system, you will develop a function that models saccades' acceleration and deceleration phases. Additionally, you will demonstrate code for detecting saccades, providing a comprehensive understanding of both simulating and identifying these rapid eye movements.



# Chapter 9: Lab Example 1



## Overview

In this lab, we will try to run a very simplistic eye-tracking exercise using MATLAB. The code we will use implements the Hough transform algorithm previously touched on, as well as an algorithm called Viola-Jones. MATLAB can use this algorithm to detect and classify faces, noses, eyes, mouths, and upper bodies. The base code is inspired and modified from this Github poster:

<https://github.com/ishitadatta/EyeballDetection>

## Objective

This laboratory exercise aims to understand how to apply eye-tracking algorithms within MATLAB to perform a simplistic eye-tracking exercise using a built-in webcam.

## MATLAB Setup

Let's discuss a basic MATLAB code to accomplish our laboratory exercise goals. Begin by clearing your workspace and any figures with the following:

```
clear all  
clf('reset');
```

As we discussed in the objectives, we are going to use the built-in webcam from an LG Gram laptop, and we can call the webcam using:

```
cam=webcam();
```

Next, we will set up some simple identifier's that tell us when the subject is looking right, left, straight, or not found (noface).

```
right=imread('RIGHT.jpg');  
left=imread('LEFT.jpg');  
noface=imread('no_face.jpg');  
straight=imread('STRAIGHT.jpg');
```

To detect the face and eyes, we are going to use the Viola-Jones algorithm with:

```
detector = vision.CascadeObjectDetector();  
detector1 =  
vision.CascadeObjectDetector('EyePairSmall');
```

Next, we define the laptop screen dimensions and camera information manually with the following definitions:

```
screenWidthCm = 50;  
screenHeightCm = 30;  
distanceToCameraCm = 60;  
cameraFoV = 60;
```

We need to create an array to store the coordinates of the eye position with respect to time, and this data will be collected for 30 seconds. The repeat variable, while true, will let us run a continuous loop of the eye tracking:

```
pupilPositions = [];  
startTime = tic;  
duration = 30;  
repeat = true;
```

Let us now define the loop that will run for the 30-second duration; this portion defines the capture of images, face and eye detection, and pupil detection via the Hough transform algorithm, defines bounding boxes gaze detection, and allows the loop to end:

```
while repeat  
    vid=snapshot(cam);  
    vid = rgb2gray(vid);  
    img = flip(vid, 2);  
  
    bbox = step(detector, img);
```

```

    if ~ isempty(bbox)
        biggest_box=1;
        for i=1:rank(bbox)
            if bbox(i,3)>bbox(biggest_box,3)
                biggest_box=i;
            end
        end
    end
    faceImage = imcrop(img,bbox(biggest_box,:));
    bboxeyes = step(detector1, faceImage);

    subplot(2,2,1),subimage(img); hold on;
    for i=1:size(bbox,1)
        rectangle('position', bbox(i, :),
'lineWidth', 2, 'edgeColor', 'y');
    end

    subplot(2,2,3),subimage(faceImage);

    if ~ isempty(bboxeyes)

        biggest_box_eyes=1;
        for i=1:rank(bboxeyes)
            if
bboxeyes(i,3)>bboxeyes(biggest_box_eyes,3)
                biggest_box_eyes=i;
            end
        end

        bboxeyeshalf=[bboxeyes(biggest_box_eyes,1),bboxeyes(biggest_box_eyes,2),bboxeyes(biggest_box_eyes,3)/3,bboxeyes(biggest_box_eyes,4)];

        eyesImage = imcrop(faceImage,bboxeyeshalf(1,:));
        eyesImage = imadjust(eyesImage);

        r = bboxeyeshalf(1,4)/4;

```

```

[centers, radii, metric] = imfindcircles(eyesImage,
[floor(r-r/4) floor(r+r/2)], 'ObjectPolarity','dark',
'Sensitivity', 0.93);
[M,I] = sort(radii, 'descend');

eyesPositions = centers;

subplot(2,2,2),subimage(eyesImage); hold
on;

viscircles(centers, radii,'EdgeColor','b');

    if ~isempty(centers)
        pupil_x=centers(1,1);
        pupil_y=centers(1,2);
        pupilPositions = [pupilPositions;
pupil_x,pupil_y];
        disL=abs(0-pupil_x);
        disR=abs(bboxeyes(1,3)/3-pupil_x);
        subplot(2,2,4);
        if disL>disR+16
            subimage(right);
        else if disR>disL
            subimage(left);
        else
            subimage(straight);
        end
    end
end

else
    subplot(2,2,4);
    subimage(noface);
end
set(gca,'XtickLabel',[],'YtickLabel',[]);
hold off;
if toc(startTime) > duration
    repeat = false;

```

```
end  
end
```

Now that we have defined most of our eye-tracking MATLAB process and data collection, we will normalize the pupil position to the screen dimensions that we previously defined. This enables us to map the gaze position on the screen (roughly). This can be accomplished with the following:

```
if ~isempty(pupilPositions)  
    imgWidth = size(vid, 2);  
    imgHeight = size(vid, 1);  
  
    normalizedPupilX = pupilPositions(:,1) / imgWidth;  
    normalizedPupilY = pupilPositions(:,2) / imgHeight;  
  
    screenPosX = normalizedPupilX * screenWidthCm;  
    screenPosY = (1 - normalizedPupilY) *  
screenHeightCm;  
end
```

We can utilize a Gaussian kernel to smooth the data that was collected:

```
kernelSize = 25;  
sigma = kernelSize / 5;  
  
[x, y] = meshgrid(linspace(-kernelSize/2, kernelSize/2,  
kernelSize), linspace(-kernelSize/2, kernelSize/2,  
kernelSize));  
gaussianKernel = exp(-(x.^2 + y.^2) / (2 * sigma^2));  
gaussianKernel = gaussianKernel / sum(gaussianKernel,  
'all');
```

This ends the eye-tracking MATLAB code segment. The commands above will detect the face, eyes, and pupils and collect an array of coordinates for their position on the screen. Let's test the command in MATLAB; it should generate a window that detects whether you look left, right, or straight! It should look like Fig. 9.4.

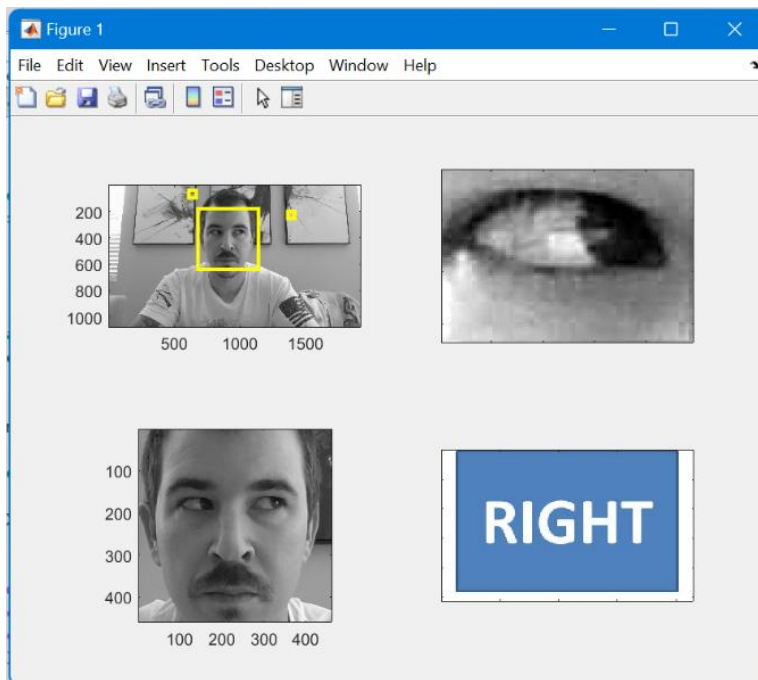


Figure 9.4: Eye Tracking

To analyze and process the data one step further, we could try to generate a heat map representing a visual estimation of gaze points on the laptop screen, as if you were looking at an image. This plot can be accomplished with:

```
if ~isempty(screenPosX) && ~isempty(screenPosY)
    gridSizeX = 100;
    gridSizeY = 100;

    [N, Xedges, Yedges] = histcounts2(screenPosX,
    screenPosY, [gridSizeX gridSizeY]);

    density = N / sum(N, 'all');
```

```

    smoothedDensity = conv2(density, gaussianKernel,
'same');

    [X, Y] = meshgrid(linspace(0, screenWidthCm,
gridSizeX), linspace(0, screenHeightCm, gridSizeY));

    figure;
    contourf(X, Y, smoothedDensity', 20);
    colormap('hot');
    colorbar;
    title('Smoothed 2D Heatmap of Gaze on Screen');
    xlabel('Screen Width (cm)');
    ylabel('Screen Height (cm)');
    axis equal;
else
    disp('No screen position data available for heatmap
generation.');
```



Figure 9.5: Smoothed 2D Heatmap

The results of running this 30-second code could produce a rough estimation of your gaze in a heat map of the screen dimensions.

To experiment with mapping my gaze while looking at an image, let's take a full-screen zoom of this chapter's title image and map my gaze while looking at the title image shown on the right:

The result, if we were to plot the heat-map as an overlay to the original image (Fig 9.6) (bottom toolbar cropped out), shows us a rough idea of how my gaze was concentrated on the image:



Figure 9.6: Heatmap on Image



## Chapter 9: Lab Example 2



Saccades are rapid, ballistic movements of the eyes that shift the point of fixation from one location to another. The human body produces these movements fastest, with peak velocities ranging from 30 to 500 degrees per second and durations typically between 20 to 200 milliseconds, depending on the amplitude. Saccades can be voluntary, such as when we look at a specific object, and involuntary, occurring reflexively in response to stimuli. Despite their speed, saccades are highly precise, allowing the eyes to land accurately on the intended target. The latency, or the time from a stimulus's appearance to the saccade's initiation, is usually around 200 milliseconds.

In eye tracking, saccades are crucial because they help identify periods of fixation when the eyes are relatively still. Researchers and designers can gain insights into what captures and holds a person's attention by analyzing these fixations. The frequency, amplitude, and duration of saccades also indicate cognitive load and attentional processes; for instance, increased saccadic activity might suggest higher cognitive processing or searching behavior. In usability studies, understanding gaze patterns and how users shift their gaze can inform improvements in interface design and overall user experience.

Saccades are integral to understanding visual perception in psychophysics,



Figure 9.7: Saccade

which explores the relationship between physical stimuli and the resulting sensations and perceptions. During saccades, vision is temporarily suppressed—a phenomenon known as saccadic suppression—enabling researchers to study how visual information is integrated across different fixations. Saccadic patterns also provide insights into attention and awareness, revealing how attention is shifted and maintained during various tasks.

Additionally, the latency and dynamics of saccades are used in reaction time studies to investigate the timing and coordination of perceptual and motor processes.

Applications of saccadic research span various fields, including neuroscience, marketing, virtual reality, and gaming. In neuroscience, abnormal saccadic movements can indicate neurological conditions such as Parkinson's disease, schizophrenia, and ADHD. In marketing, eye tracking and analysis of saccadic movements help understand consumer behavior, such as how people view advertisements or product placements. In virtual reality and gaming, eye tracking enhances user experiences by allowing systems to respond to where users are looking in real-time. Understanding and analyzing saccades provide valuable insights into attention, perception, cognitive processes, and neurological health, making them a critical component of research and technological applications.

A valuable resource for understanding the background of saccades is available at:

[SR Research Blog on Eye Tracking Terminology.](#)

In this lab, we will create MATLAB code to generate simulated saccades.

To simulate a saccade in MATLAB, we need to create a function that models an eye's rapid, ballistic movement as it shifts focus from one point to another. Their quick acceleration and deceleration phases typically characterize saccades, and the dynamics can be approximated using a second-order system. We can modify the previous script to include multiple saccades with varying amplitudes and intervals to simulate a series of saccades. Here's an updated version of the script to achieve this:

```
% Simulate a series of saccades in MATLAB

% Parameters
amplitudes = [10, -15, 20, -25, 30]; % amplitudes of the
saccades in degrees
durations = [0.05, 0.05, 0.05, 0.05, 0.05]; % durations of the
saccades in seconds
```

```

intervals = [0.1, 0.15, 0.2, 0.1]; % intervals between
saccades in seconds
sampling_rate = 1000; % samples per second

% Total time calculation
total_time = sum(durations) + sum(intervals);
t_total = 0:1/sampling_rate:total_time;

% Time vector and position initialization
eye_position = zeros(size(t_total));
current_time = 0;

% Second-order system parameters (assuming same for all
saccades)
zeta = 0.8; % damping ratio

% Loop through each saccade
for i = 1:length(amplitudes)
    % Current saccade parameters
    amplitude = amplitudes(i);
    duration = durations(i);
    omega = 2 * pi / duration; % natural frequency (rad/s)

    % Time vector for the current saccade
    t_saccade = 0:1/sampling_rate:duration;

    % System transfer function:  $G(s) = \frac{\omega^2}{s^2 + 2\zeta\omega s + \omega^2}$ 
    num = [omega^2];
    den = [1, 2*zeta*omega, omega^2];
    sys = tf(num, den);

    % Step response of the system to simulate the saccade
    [y, t_saccade] = step(sys, t_saccade);
    y = y * amplitude; % Scale the response to the desired
    amplitude

    % Update the eye position
    start_idx = find(t_total >= current_time, 1);
    end_idx = start_idx + length(y) - 1;
    eye_position(start_idx:end_idx) =
    eye_position(start_idx:end_idx) + y';

```

```

% Update current time
current_time = current_time + duration;

% Add interval between saccades if not the last saccade
if i < length(amplitudes)
    interval = intervals(i);
    current_time = current_time + interval;
end
end

% Plot the series of saccades
figure;
plot(t_total, eye_position, 'LineWidth', 2);
xlabel('Time (s)');
ylabel('Eye Position (degrees)');
title('Series of Saccades Simulation');
grid on;

% Optional: Save the plot as an image
saveas(gcf, 'series_of_saccades_simulation.png');

% Display the plot
disp('Series of saccades simulation completed.');
```

The script simulates a series of saccades with parameters that define the amplitudes (in degrees), durations (in seconds), and intervals between successive saccades (also in seconds). The simulation operates at a specified sampling rate (samples per second). To compute the total simulation time, the script sums the durations of all saccades and the intervals between them. It initializes a time vector and an eye position array to represent the total simulation period.

The script processes each saccade within a loop by defining its natural frequency ( $\omega$ ) and damping ratio ( $\zeta$ ). It computes the step response of a second-order system for each saccade, updates the eye position array with the new saccade data, and adjusts the current time to account for the duration of the saccade and the interval to the next one. Finally, the script plots the eye position over time, visualizing the series of saccades. This allows for adjusting parameters to match the specific characteristics of the simulated saccades.

Now that we can generate saccades, it would be interesting to detect them as well.

We can use a velocity-based method to detect saccades in the generated eye position data. This involves computing the velocity of the eye position and identifying points where the velocity exceeds a certain threshold, which indicates the occurrence of a saccade.

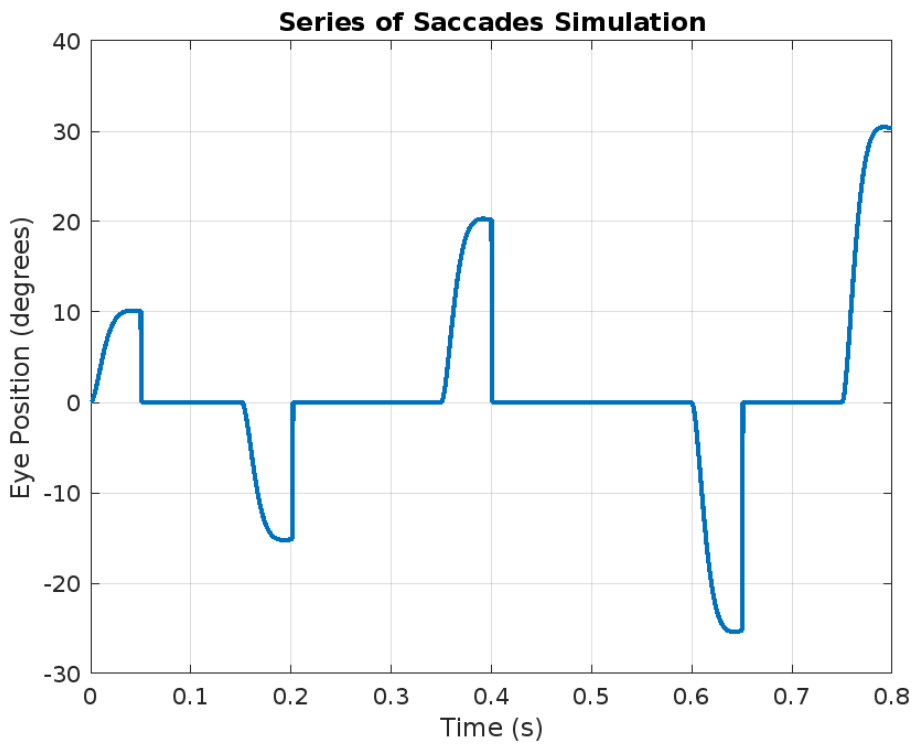


Figure 9.8: Series of Saccades Simulation

```
% Saccade detection based on generated data from the previous
script

% Parameters for saccade detection
velocity_threshold = 500; % degrees per second
```

```

% Compute the velocity of the eye position
eye_velocity = diff(eye_position) * sampling_rate; % velocity
in degrees per second
eye_velocity = [0, eye_velocity]; % pad the first element to
match the length of eye_position

% Detect saccades based on the velocity threshold
saccade_indices = find(abs(eye_velocity) >
velocity_threshold);

% Combine contiguous indices into saccades
saccade_starts = saccade_indices([1,
find(diff(saccade_indices) > 1) + 1]);
saccade_ends = saccade_indices([find(diff(saccade_indices) >
1), end]);

% Plot the detected saccades
figure;
plot(t_total, eye_position, 'LineWidth', 2);
hold on;
for i = 1:length(saccade_starts)
    saccade_time = t_total(saccade_starts(i):saccade_ends(i));
    saccade_pos =
eye_position(saccade_starts(i):saccade_ends(i));
    plot(saccade_time, saccade_pos, 'r', 'LineWidth', 2);
end
xlabel('Time (s)');
ylabel('Eye Position (degrees)');
title('Detected Saccades');
legend('Eye Position', 'Detected Saccades');
grid on;

% Optional: Save the plot as an image
saveas(gcf, 'detected_saccades.png');

% Display the results
disp('Saccade detection completed.');
```

```

disp('Detected saccades:');
for i = 1:length(saccade_starts)
    fprintf('Saccade %d: Start Time = %.3f s, End Time = %.3f
s, Amplitude = %.2f degrees\n', ...
        i, t_total(saccade_starts(i)),
t_total(saccade_ends(i)), ...

```

```

        eye_position(saccade_ends(i)) -
eye_position(saccade_starts(i));
end

```

The script begins by calculating the velocity of the eye position using the `diff` function and scales it by the sampling rate to obtain the velocity in degrees per second. The `eye_velocity` array is then padded with a zero at the start to match the length of the `eye_position` array.

For saccade detection, the script identifies indices where the absolute value of

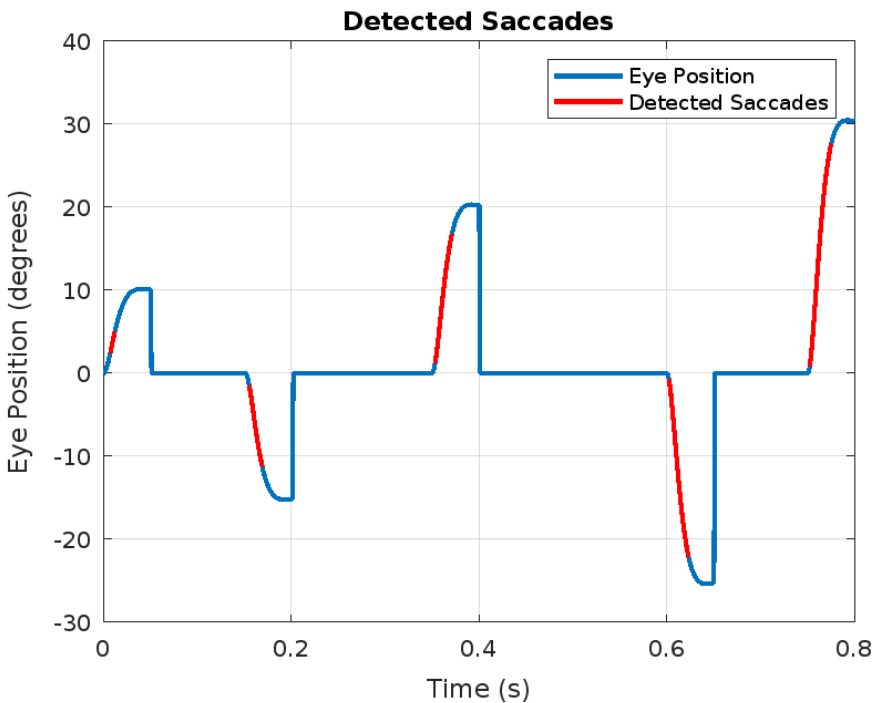


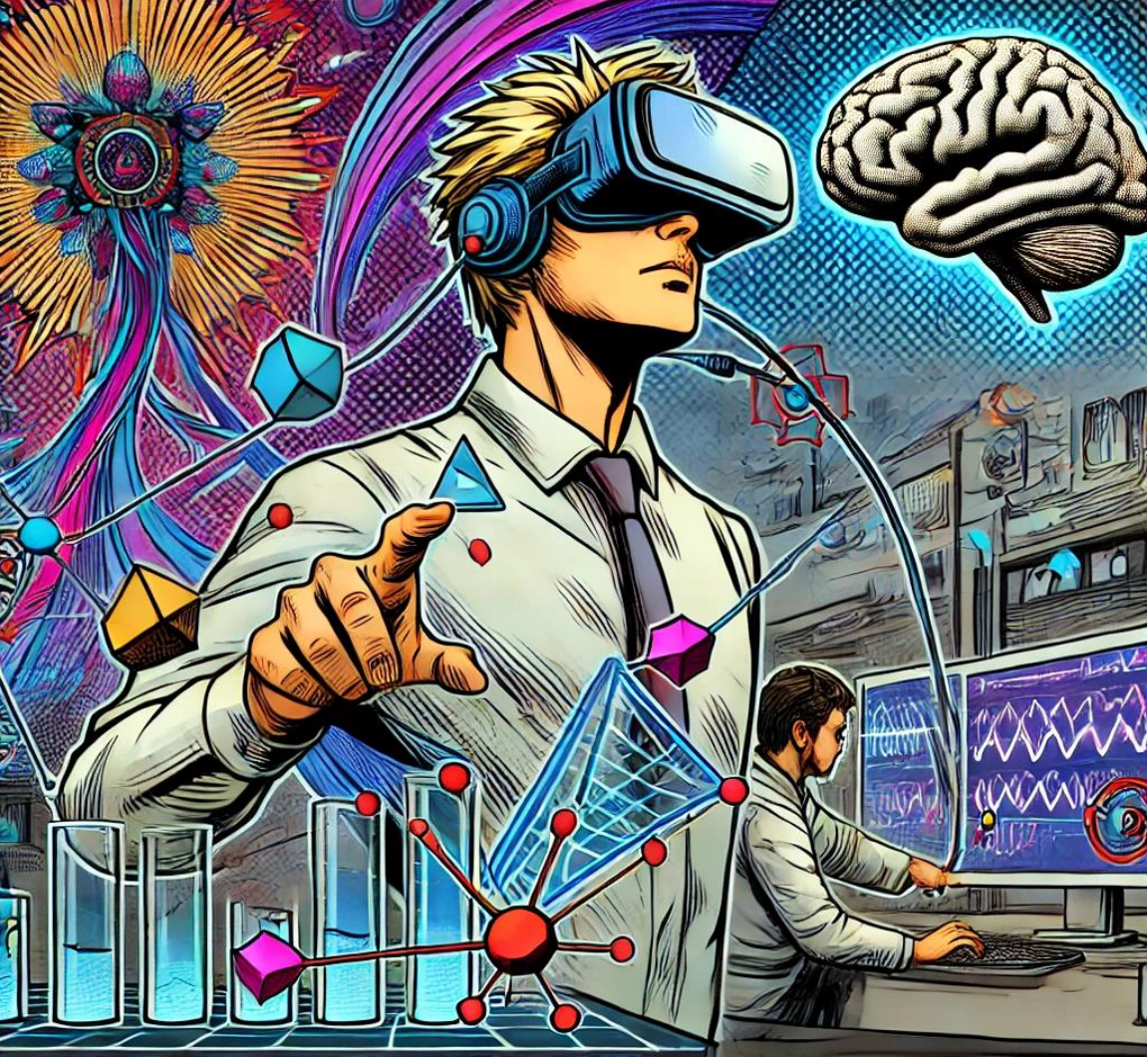
Figure 9.9: Detected Saccades

the velocity exceeds the `velocity_threshold`. Contiguous indices are grouped into individual saccades by detecting where the difference between successive indices is greater than one.

The eye position is then plotted with the detected saccades highlighted in red, and each detected saccade's start and end times are displayed in the console. Finally, the script prints each detected saccade's start time, end time, and amplitude. This script should be run after the previous script that generates the saccade data. Adjust the `velocity_threshold` as needed better to match the saccades' characteristics in your data.







## Chapter 10

# Mind Games: The Worlds of Psychophysics and Virtual Reality

# Introduction and Learning Objectives

So far in this textbook, you have explored the visual system in Chapter 8 and the use of eye trackers in Chapter 9, both of which are critical for understanding how we perceive and interact with our environment. These chapters laid the groundwork for appreciating the complex interplay between visual stimuli and perceptual responses.

In this next chapter, we will explore how to integrate psychophysics and virtual reality (VR) and how these technologies can be harnessed to advance our understanding of sensory perception. We will discuss the principles of psychophysics, the benefits of VR in psychophysical research, and the various types of psychophysical tests that can be enhanced through VR. Furthermore, we will explore trends and future directions, including multisensory experiments, computational advancements, and ethical considerations. By the end of this chapter, you will be able to:

1. *Understand the basic concepts and methodologies of psychophysics and their application in VR environments.*
2. *Identify and explain the psychophysical tests that can be conducted using VR technology.*
3. *Discuss the advantages and potential challenges of integrating VR into psychophysical research.*
4. *Explore the latest trends and future directions in psychophysics, including multisensory experiments and computational models.*
5. *Recognize the ethical considerations involved in conducting psychophysical research in immersive VR settings.*

## Introduction to Psychophysics

### *Definition and Scope of Psychophysics*

Psychophysics is the scientific study of the relationship between physical stimuli and the sensations and perceptions they evoke. It aims to quantify the link between objective stimulus properties and subjective sensory experiences, enabling a deeper understanding of how we perceive the world around us.

## ***Historical Overview***

The origins of psychophysics date back to the mid-19th century with the pioneering work of Gustav Fechner, who is often regarded as the father of psychophysics (Fig. 10.1 [208]) [209]. Fechner's law, which describes the logarithmic relationship between stimulus intensity and sensation, was a significant breakthrough. Other key contributors include Ernst Weber, known for Weber's Law, which quantifies the smallest noticeable difference in stimulus intensity, and S.S. Stevens, who developed the concept of Stevens' power law, addressing the relationship between stimulus magnitude and perceived intensity [210].

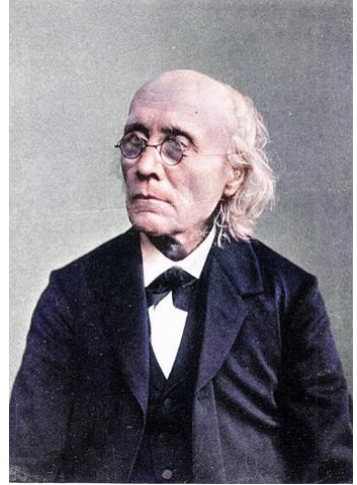


Figure 10.1: Gustav Theodore Fechner (1801–1887) [208]

# **Fundamentals of Psychophysical Methods**

## ***Basic Concepts***

Psychophysics explores the connection between stimuli and our sensory perceptions. Two essential concepts in this field are thresholds and sensitivity. The absolute threshold is the minimum intensity of a stimulus that can be detected. In contrast, the difference threshold (or just noticeable difference, JND) is the slightest change in stimulus intensity that can be detected. Sensitivity refers to the ability to detect these thresholds (Fig. 10.2 [211]). The psychometric function (Fig. 10.3 [212]) illustrates these relationships, showing how response probability changes with stimulus intensity, highlighting low and high-sensitivity regions [213].

## ***Common Psychophysical Paradigms***

In psychophysical experiments, three primary methods are used to explore sensory thresholds and responses (Fig. 10.3 [214]).

# Absolute Threshold

The weakest amount of a stimulus that a person can detect 50% of the time.

|         |                                                                                   |                                                                 |
|---------|-----------------------------------------------------------------------------------|-----------------------------------------------------------------|
| Sight   |  | Seeing a candle flame 30 miles away on a clear night            |
| Hearing |  | Hearing a watch ticking 20 feet away                            |
| Touch   |  | Feeling a bee's wing falling a distance of 1cm onto your cheek  |
| Smell   |  | Smelling one drop of perfume in a three room house              |
| Taste   |  | Tasting one teaspoon of sugar dissolved in two gallons of water |

Figure 10.2: The absolute threshold represents the weakest amount of a stimulus that a person can detect 50% of the time. Examples include seeing a candle flame 30 miles away on a clear night, hearing a watch ticking 20 feet away, feeling a bee's wing falling on the cheek from 1 cm, smelling one drop of perfume in a three-room home, and tasting one teaspoon of sugar in two gallons of water. [211]

## ***Method of Limit***

This approach involves gradually increasing or decreasing stimuli. For instance, a light might be dimmed or brightened step by step until the participant indicates whether they can or cannot detect it. This helps determine the point of detection or absolute threshold [215].

## ***Method of Adjustment***

Participants have control over the stimulus intensity. They adjust it themselves until they can detect the stimulus. This method is often quicker and can provide immediate feedback on threshold levels [215].

### ***Method of Constant Stimuli***

This method randomly presents stimuli of varying intensities. The participant indicates whether they detect each stimulus. This comprehensive method allows for the creation of a detailed psychometric function that shows the probability of detection across different stimulus intensities [215].

### ***Advantages of Using VR in Psychophysics***

Virtual Reality (VR) significantly enhances psychophysical research by offering a controlled and immersive environment. One of the key benefits is improved control over stimuli, allowing researchers to manipulate virtual environments with high precision and ensuring consistent and replicable experimental conditions [187]. Additionally, VR provides a strong sense of immersion, making experimental tasks more engaging and realistic for participants. Another advantage is the ability to recreate VR environments,

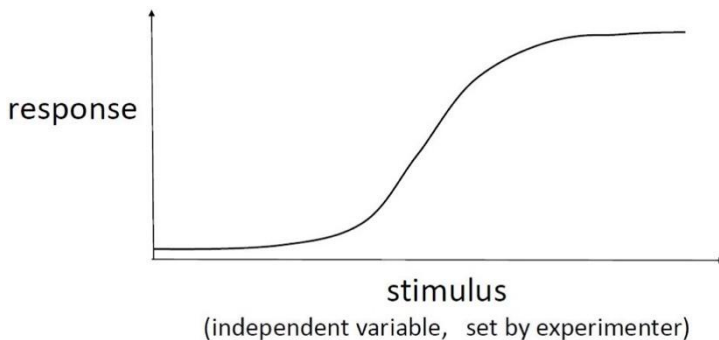


Figure 10.3: The psychometric function illustrates the relationship between stimulus intensity (the independent variable set by the experimenter) and the response. The sigmoidal shape of the curve demonstrates regions of low and high sensitivity, showing how small changes in stimulus intensity can produce significant changes in response at intermediate intensities. This function is crucial for understanding absolute and difference thresholds in psychophysics. [214]

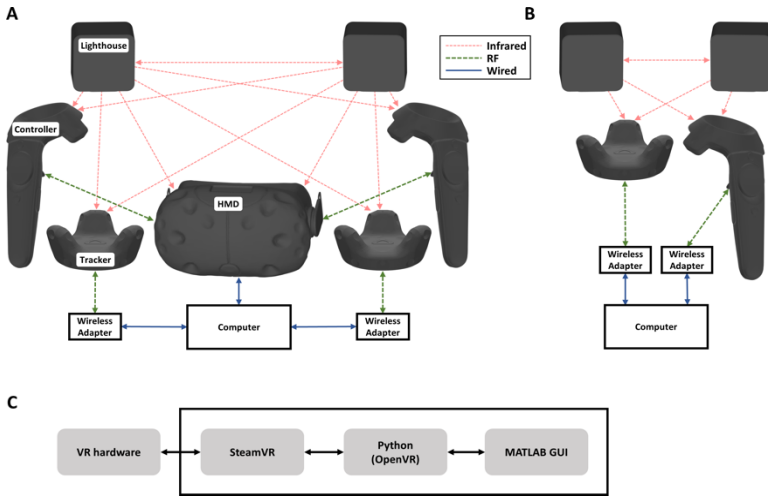


Figure 10.4: A detailed VR setup for psychophysics experiments. The system includes hardware components such as VR headsets (HMDs), controllers, lighthouses for positional tracking, and wireless adapters, all interconnected via infrared, RF, and wired connections. The setup is managed by a central computer. The software workflow involves VR hardware integration through SteamVR, interfaced with Python (OpenVR), and controlled via a MATLAB GUI for precise experimental design and data analysis. [217]

which can be exactly reproduced across different sessions and participants, ensuring the consistency and reliability of experimental conditions [216].

### ***VR Technologies in Psychophysics***

VR technology in psychophysics integrates various hardware and software components to create immersive and precise experimental environments.

The hardware (Fig. 10.4 [217]) comprises VR head-mounted displays (HMDs), motion tracking systems, haptic devices, and specialized controllers that enhance sensory feedback and interaction [218]. The setup often involves devices such as lighthouses for positional tracking, controllers for input, and wireless adapters for connectivity, all coordinated by a central computer.

On the software side, VR platforms and simulation software, such as SteamVR and custom Python scripts, are tailored for psychophysical experiments. These tools allow researchers to design, control, and analyze sensory stimuli within virtual environments, providing detailed and replicable experimental data [218].

## *Case Studies*

VR technology is increasingly utilized in psychophysics to investigate sensory perceptions and cognitive processes. Various case studies illustrate VR's diverse applications and benefits in this field.

One notable case study involves using VR to examine the visual perception of surface materials. Researchers utilized VR to manipulate visual cues such as texture, glossiness, and reflectance properties, providing insights into how these factors influence material perception under different lighting conditions. This study highlighted the ability of VR to create controlled, immersive environments for detailed psychophysical experiments [219].

Another application of VR in psychophysics is in the realm of exposure therapy for anxiety and post-traumatic stress disorder (PTSD). VR exposure therapy allows patients to engage with virtual environments that simulate anxiety-inducing scenarios in a controlled and safe manner. This method has significantly reduced symptoms by enabling repeated and consistent exposure without the constraints of real-world settings [219].

Furthermore, VR has been used to investigate human behavior and cognitive functions. For example, the Unity Experiment Framework (UXF) leverages VR to study spatial cognition and navigation. By immersing participants in virtual mazes or landscapes, researchers can manipulate variables such as spatial layout and environmental cues to observe their effects on navigation and memory. This approach offers precise control over experimental conditions and the ability to measure responses accurately [219].

Training and education also benefit from VR's immersive capabilities. Hydro One and Avangrid have implemented VR training programs to enhance employees' skills and safety procedures [220]. These programs simulate real-world scenarios, allowing trainees to practice responses to various situations without the risks associated with on-the-job training. The interactive and engaging nature of VR training has proven to increase retention and performance in trainees [219].

These case studies demonstrate the versatility and effectiveness of VR in advancing psychophysical research and applications, providing valuable

insights into sensory processing, cognitive functions, and therapeutic interventions.

## **Types of Psychophysical Tests**

### ***Visual Psychophysics***

Visual psychophysics studies the relationship between physical stimuli and the perceptual experiences they produce, focusing on how the visual system interprets and processes various aspects of light and color. One of the key areas of study is contrast sensitivity, which refers to the ability to detect differences in luminance between an object and its background. This ability is vital for activities like night driving, where low light conditions make it difficult to see objects unless they contrast sharply with their surroundings. High contrast sensitivity is also essential for reading, allowing for a clear distinction between text and background. Another critical area is color discrimination, which assesses an individual's ability to differentiate between various hues. This is particularly important in professions requiring color accuracy, such as graphic design, quality control in manufacturing, or even medical diagnostics, where subtle color differences might indicate a condition or issue. Visual acuity, another cornerstone of visual psychophysics, measures the clarity or sharpness of vision. It is fundamental for tasks that require attention to detail, such as reading fine print, recognizing faces, or driving. Visual acuity is often tested using standardized charts that measure how well someone can discern letters or symbols at a given distance.[221].

### ***Auditory Psychophysics***

Auditory psychophysics explores the relationship between acoustic stimuli and auditory perception, investigating how the auditory system processes sound. A primary focus is determining auditory thresholds, the quietest sounds an individual can detect. These thresholds are crucial in diagnosing hearing impairments and are commonly tested using pure tone audiometry. Identifying these thresholds helps fit hearing aids and other assistive listening devices. Another important aspect of auditory psychophysics is sound localization, which determines where a sound originates in space. This skill is essential for

effective communication in noisy environments, as it allows individuals to focus on a speaker's voice amid background noise. Moreover, sound localization is vital for spatial awareness, helping people navigate environments safely and effectively, whether crossing a street or detecting potential hazards [222].

### ***Olfactory and Gustatory Psychophysics***

Olfactory and gustatory psychophysics examine the senses of smell and taste, respectively, and their importance in daily life. Olfactory sensitivity involves detecting and identifying various odors critical for safety and quality of life. For instance, the ability to smell gas leaks, smoke, or spoiled food can prevent accidents and health risks. Additionally, olfactory sensitivity plays a significant role in flavor perception, as the sense of smell is closely linked with taste, contributing to the overall experience of food and beverages. On the other hand, Gustatory psychophysics focuses on understanding taste and distinguishing between different taste qualities—sweet, sour, bitter, salty, and umami. This ability is crucial for maintaining a balanced diet, as it influences food preferences and nutritional intake. Moreover, taste sensitivity is important in the culinary arts, where subtle flavor distinctions can impact the outcome of a dish. Both olfactory and gustatory sensitivities can diminish with age or due to certain medical conditions, affecting quality of life [223].

### ***Somatosensory Psychophysics***

Somatosensory psychophysics investigates the sense of touch, including how the body perceives physical sensations such as pressure, vibration, pain, and temperature. Tactile sensitivity is a key study area, focusing on detecting delicate touch and texture. This sensitivity is crucial for tasks that require fine motor skills, such as writing, using tools, or manipulating small objects. It also plays a significant role in perceiving the physical properties of objects, such as softness, roughness, or slipperiness. Pain perception is another critical area involving the assessment of pain threshold (the minimum stimulus that causes pain) and pain tolerance (the maximum intensity of pain an individual can endure). Understanding pain perception is essential for diagnosing and treating chronic pain conditions and developing effective pain management strategies

in clinical settings. Temperature sensitivity examines the ability to detect temperature changes, which is necessary for thermal regulation and avoiding harmful environments. For example, sensing extreme heat or cold prevents burns, frostbite, or other injuries [224].

## **Current Trends and Future Directions in Psychophysics**

### ***Integrating Multisensory Experiments***

Recent psychophysics research increasingly focuses on integrating multiple sensory modalities to comprehensively understand how they interact and influence perception. Traditional psychophysical experiments often isolated one sense, such as vision or hearing, to study its characteristics. However, real-world sensory experiences typically involve the simultaneous processing of information from multiple senses. For instance, flavor perception involves taste and smell, while navigating through an environment requires the integration of visual, auditory, and vestibular inputs.

Fig. 10.5 [225] illustrates this multisensory approach by presenting two experiments with varying reliability conditions for visual, auditory, and tactile stimuli [225]. Experiment 1a includes conditions with low and medium auditory (LV-MA) and high visual and medium auditory (HV-MA) conditions. Experiment 1b expands this to three reliability conditions: high visual, medium auditory, and low tactile (HV-MA-LT); low visual, medium auditory, and high tactile (LV-MA-HT); and low visual, medium auditory, and low tactile (LV-MA-LT). These setups aim to understand how sensory inputs are weighted and integrated under varying reliability conditions [225].

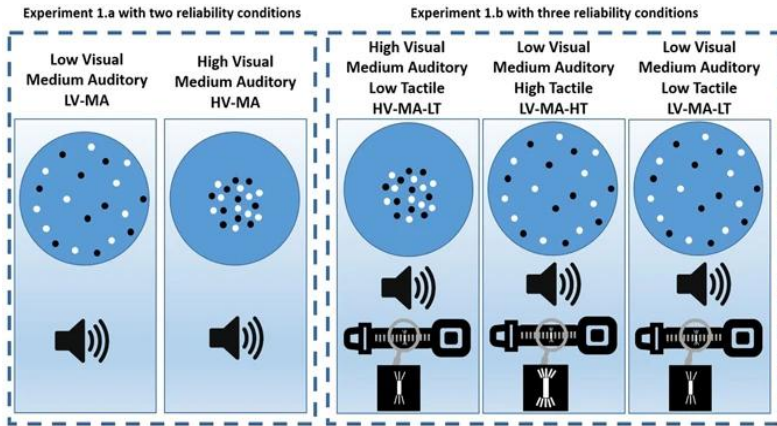


Figure 10.5: Multisensory experiments from Mahani et al. showing varying reliability conditions for visual, auditory, and tactile stimuli. Experiment setups include combinations of high, medium, and low reliability to study sensory integration. [225]

By designing experiments considering these multisensory interactions, researchers aim to uncover more accurate models of human perception and understand how the brain integrates and prioritizes different sensory inputs. This holistic approach can lead to new insights into sensory processing and its applications in virtual reality, augmented reality, and sensory rehabilitation.

### ***Ethical Considerations***

The immersive and often highly realistic nature of VR in psychophysical research introduces a range of ethical considerations. One primary concern is ensuring that participants give informed consent and fully understand the potential risks and benefits of participating in VR studies. VR is a complex and relatively new technology for many participants, which means that researchers must take extra steps to ensure that participants fully understand what VR entails. This includes explaining how the VR system works, the nature of the simulations they will experience, and the specific tasks they will be asked to perform. Additionally, researchers must communicate the potential benefits and risks of participating in VR studies. For example, while VR can provide valuable insights into cognitive processes or therapeutic benefits, there are risks, such as motion sickness, disorientation, or psychological discomfort.

Participants must be fully aware of these possibilities before consenting to participate in the study. It is crucial to emphasize that participation in VR research is voluntary, and participants can withdraw from the study at any time without penalty. Given the immersive nature of VR, which can sometimes be overwhelming, participants should feel empowered to stop the experience if they feel uncomfortable. VR environments can collect a wide range of data beyond what is typically gathered in traditional research settings. This includes detailed tracking of movements, gaze patterns, physiological responses (such as heart rate and galvanic skin response), and even voice and facial expressions. This data can provide deep insights into participant behavior and raise significant privacy concerns. Researchers must implement robust measures to protect the privacy of participants. This includes anonymizing the data wherever possible to prevent it from being traced back to individual participants. Data security protocols must be in place to protect against unauthorized access, breaches, or data misuse. Encryption and secure storage solutions are essential to maintaining data integrity and confidentiality. The extensive data collected in VR studies must be used responsibly. Researchers should be transparent about how the data will be used, who will access it, and for what purposes. Participants should be informed about any potential future uses of their data, including whether it might be shared with other researchers or used in subsequent studies [226].

Additionally, the highly immersive nature of VR can lead to various psychological effects, some of which may be adverse. For instance, participants might experience stress, anxiety, or even a sense of detachment from reality after prolonged exposure to certain VR environments. Scenarios that involve heights, confined spaces, or intense simulations can be particularly challenging for some individuals. To mitigate these risks, researchers should pre-screen participants for any conditions that might make them more vulnerable to adverse effects, such as a history of anxiety disorders, motion sickness, or vertigo. During the study, participants should be closely monitored for signs of distress, and protocols should be in place to immediately intervene if a participant experiences discomfort. After the VR experience, participants should undergo a thorough debriefing session to discuss their experience and

any lingering effects. Providing psychological support or referrals to counseling services may be necessary for participants who experience significant stress or anxiety as a result of the VR study. Given the relatively new use of VR in research, there is a need for comprehensive ethical guidelines that specifically address the challenges associated with VR. These guidelines should be developed in consultation with ethicists, psychologists, and other stakeholders to cover aspects such as informed consent, data privacy, and the psychological impact of VR. Ethical protocols for VR studies should be rigorously reviewed by Institutional Review Boards (IRBs) or ethics committees. These bodies should assess whether the study design adequately protects participants' rights and well-being and whether the potential benefits of the research justify any risks involved. As VR technology and applications evolve, so should the ethical guidelines governing its research use. Ongoing ethical review and protocol updates are necessary to address new challenges, ensuring participant safety and well-being remain the top priority [227].

While short-term use of VR in controlled settings is generally safe, the long-term effects of repeated or prolonged exposure to immersive environments are not yet fully understood. Researchers should be cautious in designing studies that require extended use of VR and consider the potential cumulative effects on participants' mental health and perception. VR's ability to create highly realistic simulations presents additional ethical considerations. For instance, using VR to simulate traumatic events or highly stressful situations could have profound psychological impacts. Researchers must balance the need for realism with the ethical imperative to avoid causing harm. In cases where realistic simulations are necessary, extra care must be taken to screen participants and provide support.

VR in psychophysical research presents exciting possibilities for understanding human behavior and cognition in immersive environments. However, it also introduces various ethical challenges that must be carefully managed to protect participants. Ensuring informed consent, safeguarding privacy, monitoring psychological impact, and adhering to strict ethical guidelines are all crucial components of conducting responsible and ethical VR research. As VR technology continues to advance, the ethical frameworks

surrounding its use in research must evolve accordingly, ensuring that the benefits of this powerful tool are realized without compromising the well-being of participants.

## **Future Work**

Recent trends in psychophysics and VR are showing promising applications for individuals with autism spectrum disorder (ASD) and Parkinson's Disease. For individuals with ASD, VR provides controlled environments to practice social interactions and develop communication skills without the unpredictability of real-life situations. Studies have shown that VR can help improve social cognition and reduce anxiety in social settings for individuals with ASD [228], [229], [230]. Future work aims to refine these VR applications to cater to specific needs and to integrate real-time feedback mechanisms to enhance the effectiveness of these interventions.

For Parkinson's Disease, VR is used to develop rehabilitation programs that help improve motor skills and balance. VR environments can simulate various physical activities and provide immediate feedback, assisting patients in practicing and improving their movements safely. Research has demonstrated that VR-based therapy can enhance motor function and reduce symptoms of Parkinson's Disease. Future directions involve integrating more personalized and adaptive VR systems that can adjust the difficulty level based on the patient's progress, ensuring a more tailored rehabilitation experience [229].

These advancements highlight VR's potential to create engaging and effective therapeutic environments, offering new hope for individuals with ASD and Parkinson's Disease. Continued research and development will lead to even more sophisticated and beneficial applications.

## **Chapter 10: Summary**

Promising applications of VR in psychophysics include therapeutic interventions for Autism Spectrum Disorder (ASD) and Parkinson's Disease. For ASD, VR provides controlled environments to practice social interactions and develop communication skills, reducing anxiety and improving social

cognition. For Parkinson's Disease, VR rehabilitation programs help improve motor skills and balance, enhancing motor function and symptom reduction. Future work aims to refine VR applications with real-time feedback and adaptive systems, offering personalized therapeutic environments. These advancements will shape the future of psychophysics, providing new insights and effective treatments for sensory and cognitive disorders.

Chapter 10 explored the integration of psychophysics and Virtual Reality (VR), highlighting how VR transforms our sensory perception understanding. Traditionally, psychophysical tests have been conducted in controlled, static environments to isolate specific sensory responses. VR has revolutionized this approach by providing dynamic, immersive environments replicating real-world conditions while maintaining experimental control.

VR enhances psychophysical research by enabling complex, multi-sensory experiences that are otherwise impractical to recreate. Researchers can simulate diverse environments, examine sensory interactions, and tailor experiments to individual participants. Key trends include multisensory studies, advancements in computational power, and emerging ethical considerations in VR research. Promising VR applications in psychophysics include therapeutic interventions for Autism Spectrum Disorder (ASD) and Parkinson's Disease. For ASD, VR offers controlled environments for practicing social interactions, improving communication skills, and reducing anxiety. For Parkinson's Disease, VR-based rehabilitation programs help improve motor skills and balance, leading to better symptom management and quality of life.

Looking ahead, the refinement of real-time feedback and adaptive systems within VR holds great potential for personalized therapeutic environments. These advancements will shape the future of psychophysics, offering new insights and effective treatments for sensory and cognitive disorders.

Having explored the intersection of VR and psychophysics, we now focus on the auditory system. In the next chapter, you will learn about the auditory system, and we will explore how the auditory system processes sound, including pitch, loudness, and spatial location. Through this exploration, you will gain a deeper understanding of how hearing is measured and analyzed

using psychophysical methods and the implications this has for both research and clinical practice.



## Chapter 10: Learning activities

### Learning Activity 10.1

#### *Brainstorming Psychophysics Paradigms*

##### *Objective*

Students will collaboratively brainstorm and compile a comprehensive list of known psychophysics paradigms and descriptions of what each paradigm tests.

##### *Materials*

- Whiteboard or flip chart
- Markers
- Internet access (for research)
- Computers or tablets
- Note-taking materials (paper, pens, or digital tools)

##### *Time*

20-30 minutes

##### *Instructions*

###### *Introduction (3 minutes):*

1. Introduce the activity and explain its goal: to brainstorm and compile a list of psychophysics paradigms and what they test.
2. Briefly explain a psychophysics paradigm's importance in understanding sensory perception and cognitive processes.

###### *Individual Brainstorm (5 minutes):*

3. Instruct students to individually brainstorm and list as many psychophysics paradigms as possible. Encourage them to think about what each paradigm tests.

###### *Peer Share (5 minutes):*

4. Have students pair and share their lists, combining their knowledge to expand them.



***Group Compilation (10 minutes):***

5. Form small groups of 4-5 students. Each pair will join another pair. 6. In these groups, students will combine their lists and organize the paradigms into a comprehensive list detailing what each paradigm tests. 7. Provide large sheets of paper or poster boards and markers for the groups to write down their combined lists.

***Class Presentation and Compilation (7-10 minutes):***

8. Each group will present their compiled list to the class. 9. As each group presents, compile a master list on the whiteboard or flip chart to avoid duplicates and include all unique paradigms.

***Conclusion (2 minutes):***

10. Summarize the key points and the final comprehensive list of psychophysics paradigms, emphasizing the variety and scope of what each paradigm tests. 11. Encourage students to reflect on the importance of these paradigms in psychophysical research and their applications.

***Some Examples of Psychophysics Paradigms:***

***1. Signal Detection Theory (SDT)***

**What it Tests:** Assesses the ability to distinguish between signal (stimulus) and noise (non-stimulus) under conditions of uncertainty. It measures sensitivity ( $d'$ ) and response bias (criterion).

***2. Method of Limits***

**What it Tests:** Determines the threshold at which a stimulus is detected. It involves gradually increasing or decreasing the intensity of a stimulus until the subject can detect it.

***3. Method of Constant Stimuli***

**What it Tests:** Establishes the sensory threshold by randomly presenting stimuli of varying intensities and recording the detection frequency.

#### ***4. Method of Adjustment***

**What it Tests:** Allows the subject to control the intensity of a stimulus, adjusting it until it is barely detectable. This method finds the just-noticeable difference (JND) or absolute threshold.

#### ***5. Two-Alternative Forced Choice (2AFC)***

**What it Tests:** Participants are presented with two options and must choose which contains the target stimulus. This method helps to reduce response bias and measure sensory discrimination.

#### ***6. Staircase Procedure***

**What it Tests:** Adaptive method where the stimulus intensity is adjusted based on the subject's responses. If the subject detects the stimulus, the intensity is decreased; if not, it is increased. This method converges on the threshold level.

#### ***7. Magnitude Estimation***

**What it Tests:** Participants assign numerical values to the perceived intensity of a stimulus. This method is used to study the relationship between stimulus intensity and perceived magnitude.

#### ***8. Cross-Modal Matching***

**What it Tests:** Involves comparing the intensity of stimuli across different sensory modalities (e.g., matching the loudness of a sound to the brightness of a light). This method explores sensory integration and perception.

#### ***9. Forced-Choice Staircase***

**What it Tests:** Combines forced-choice methodology with the staircase procedure. Participants are given multiple trials with varying stimulus intensities, and the intensity is adjusted based on correct or incorrect responses.

#### ***10. Temporal Order Judgment (TOJ)***

**What it Tests:** Assesses the ability to perceive the order of two stimuli presented in quick succession. This paradigm is used to study temporal resolution and processing.

### ***11. Visual Search Task***

**What it Tests:** Measures how quickly and accurately a participant can find a target stimulus among a set of distractors. This paradigm tests attention and perceptual processes.

### ***12. Contrast Sensitivity***

**What it Tests:** Determines the minimum contrast needed to detect a pattern. This method is used to study visual acuity and sensitivity to contrast.

### ***13. Lateral Masking***

**What it Tests:** Examines the effect of surrounding stimuli (masks) on the perception of a target stimulus. This paradigm investigates spatial interactions and inhibitory processes in perception.

---

## **Learning Activity 10.2**

### ***Designing a Psychophysics Experiment***

#### ***Objective***

Students will design a psychophysics experiment related to their classroom project, present a functional block diagram, and write pseudo-code for the experiment.

#### ***Materials***

- Computers or tablets
- Drawing materials (paper, markers) or diagramming software
- Note-taking materials
- Reference materials (textbooks, research articles)
- Presentation tools (PowerPoint, poster boards)

#### ***Time***

50-60 minutes



## ***Instructions***

### ***Introduction (5 minutes):***

1. Introduce the activity and explain its goal: to design a psychophysics experiment related to the classroom project, create a functional block diagram, and write pseudocode.
2. Briefly review the key components of a psychophysics experiment, functional block diagrams, and pseudocode.

### ***Brainstorming and Planning (10 minutes):***

3. Have students brainstorm ideas for their psychophysics experiment. Encourage them to think about what aspect of perception they want to study and how it relates to their classroom project.
4. Ask students to outline the main components of their experiment, including stimuli, tasks, measurement methods, and expected outcomes.

### ***Designing the Experiment (15-20 minutes):***

5. Instruct students to create a functional block diagram of their experiment. This diagram should include all major components and the flow of the experiment.
6. Provide examples of functional block diagrams if necessary and assist students as they work on their designs.

### ***Writing Pseudocode (10-15 minutes):***

7. Have students write pseudocode for their experiment, detailing the sequence of steps, data collection methods, and any computational processes involved.
8. Provide examples of pseudocode and offer guidance as needed.

### ***Group Presentation Preparation (5 minutes):***

9. Allow students to prepare a brief presentation of their experiment design, including the functional block diagram and pseudocode. They should be ready to explain their choices and the overall flow of the experiment.

### ***Presentations and Feedback (15-20 minutes):***

10. Have each student present their experiment design to the class.

11. Encourage peer feedback and constructive criticism to help refine the experiments.

***Conclusion (5 minutes):***

12. Summarize the activity and highlight key points from the presentations.
13. Emphasize the importance of careful experimental design and the role of functional block diagrams and pseudocode in planning and executing psychophysics experiments.



## Chapter 10: Lab introduction

In this series of lab exercises, you will explore advanced techniques used in psychophysics research through practical applications using MATLAB. These labs will provide hands-on experience with virtual reality (VR) and Psychtoolbox, allowing you to deepen your understanding of how these tools can be applied in psychological experiments.

In the first lab, you will be introduced to the use of VR in psychophysics research by interacting with a simple VR world using MATLAB. This exercise will guide you through loading a VRML (Virtual Reality Modeling Language) world, opening it in a VR viewer, and interacting with basic objects within the VR environment. This will help you understand how VR can be utilized to create controlled, immersive environments for psychological experiments.

In the second lab, you will explore Psychtoolbox and apply your knowledge through a practical task. Specifically, you will implement a working memory task inspired by the visual working memory capacity experiment conducted by Vogel and Machizawa (2004). This exercise will provide you with experience in setting up and conducting a psychological experiment using Psychtoolbox, enhancing your skills in experimental design and data analysis in the field of psychophysics.



# Chapter 10: Lab Example 1

## Overview

This lab exercise aims to introduce students to virtual reality (VR) in psychophysics research by interacting with a simple VR world using MATLAB. The exercise will guide students through loading a VRML (Virtual Reality Modeling Language) world, opening it in a VR viewer, and interacting with basic objects within the VR environment.



## Requirements

- MATLAB software
- Virtual Reality Toolbox
- VRML world file ('simple\_world.wrl')
- Provided MATLAB code

## Part 1: Setting Up the VR Environment

### Step 1: Preparing MATLAB

Ensure the MATLAB Virtual Reality Toolbox is installed and configured on your system.

### Step 2: Creating the VRML World

Create a simple VRML world file ('simple\_world.wrl'). This file should contain basic objects such as a table and a ball.

```
simple_world.wrl:
```wrl
VRML V2.0 utf8
WorldInfo {
    title "Simple World"
}

Background {
    skyColor [0.8 0.8 1.0]
}

Transform {
```

```

translation 0 0 0
children [
  Shape {
    geometry Box { size 4 0.2 4 }
    appearance Appearance {
      material Material { diffuseColor 0.8 0.1 0.1 }
    }
  }
  Transform {
    translation 0 1 0
    children [
      Shape {
        geometry Sphere { radius 0.5 }
        appearance Appearance {
          material Material { diffuseColor 1 1 1 }
        }
      }
    ]
  }
]
}

```

## ***Part 2: Interacting with the VRML World in MATLAB***

### ***Step 3: Loading the VRML World***

Use the provided MATLAB code to load and open the VRML world in a VR viewer. MATLAB Code:

```

% Load the VRML world
vrWorld = vrworld('simple_world.wrl');

% Open the VRML world
open(vrWorld);

% Create a viewer window for the VRML world
vrFigure = vrfigure(vrWorld);

```

#### ***Step 4: Running the Code***

1. Save the provided VRML code in a `'simple_world.wrl'` file.
2. Open MATLAB and navigate to the directory containing `'simple_world.wrl'`.
3. Copy and paste the MATLAB code into the MATLAB command window or script file.
4. Run the MATLAB code to load the VRML world and open the VR viewer.

#### ***Step 5: Exploring the VR Environment***

Interact with the VRML world using the VR viewer controls. The VR world should look like the image provided, featuring a simple setup with a red table and a white ball on top of it against a light blue background.

Observe the simple objects (table and ball) and their properties.

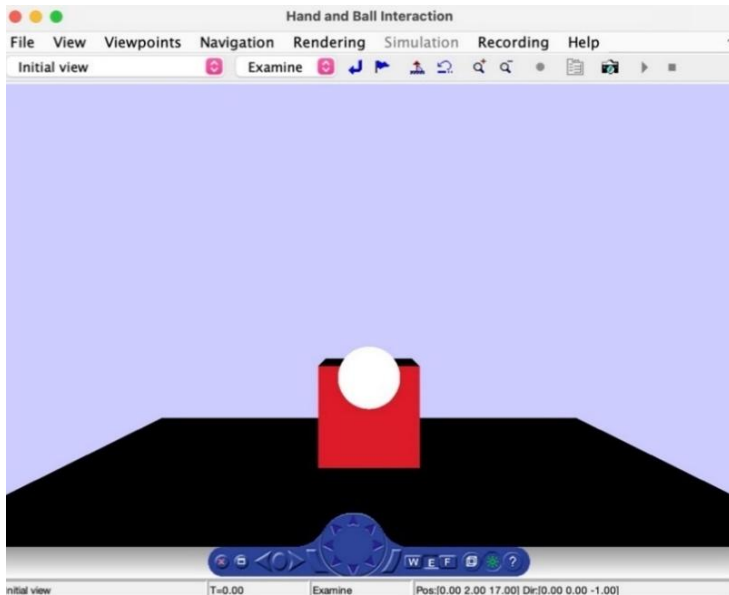


Figure 10.6: Hand and Ball Interaction

## ***Part 3: Experimentation***

### ***Step 6: Modifying the VRML World***

Modify the `simple\_world.wrl` file to change the properties of the objects (e.g., color, size, position). Reload the VRML world in MATLAB to see the changes.

### ***Step 7: Recording Observations***

Note how different properties of the objects (such as size and color) affect your perception in the VR environment. What are the potential applications of VR in psychophysical experiments, such as studying the perception of size, color, and spatial relationships?

## ***Conclusion***

This lab exercise introduced you to the basics of using VR in psychophysics research. You learned how to create a simple VRML world, load it into MATLAB, and interact with it using a VR viewer. By modifying the VR environment and observing the changes, you gained insights into the potential applications of VR for studying sensory perception.

## ***Further Reading***

- MATLAB Documentation on Virtual Reality Toolbox: [MATLAB VR Toolbox] (<https://www.mathworks.com/help/sl3d/>)
- VRML and X3D Specifications: [Web3D Consortium] (<https://www.web3d.org/>)



## Chapter 10: Lab Example 2



In this lab, we will explore [Psychtoolbox](#) and apply our knowledge through a practical task. Specifically, we will implement a working memory task inspired by the visual working memory capacity experiment conducted by *Vogel and Machizawa (2004)*. You can access the original research article at <https://www.nature.com/articles/nature02447>.

Psychtoolbox is a collection of free software tools that facilitates designing and implementing precise and complex visual and auditory stimuli for psychological experiments. It is widely used in psychology, neuroscience, and vision research. Here are some key features and components of Psychtoolbox:

- **Platform Compatibility:** Psychtoolbox is primarily used with MATLAB and GNU Octave, making it accessible to users who prefer different programming environments.
- **Stimulus Presentation:** It allows for creating and controlling visual and auditory stimuli with high temporal and spatial precision. This is crucial for experiments requiring exact timing and synchronization.
- **Graphics and Sound:** Psychtoolbox includes functions for generating and manipulating graphics, images, and sounds. This allows researchers to create complex visual displays and auditory sequences.
- **Hardware Interaction:** It supports interaction with various hardware devices such as eye trackers, response boxes, and other input/output devices, enabling comprehensive experimental setups.
- **Open Source:** Being an open-source toolkit, Psychtoolbox is freely available and can be modified to suit specific research needs.
- **Community Support:** A strong community of users and developers contribute to the toolbox, provide support, and share scripts and solutions.

Psychtoolbox is particularly powerful in experiments that require precise control over stimulus timing and presentation, such as studies in visual perception, auditory processing, and reaction time measurement.

It is available for both MATLAB and Octave. This powerful tool offers a range of commands that simplify the process of creating experiments. For more information about the available functions, visit [Psychtoolbox Documentation](#).

After installing Psychtoolbox in MATLAB, you can begin designing your experiments. In this instance, we will use an implementation provided by [Marvin Theiss](#).

### *Working memory experiment*

The visual working memory capacity experiment conducted by Vogel and Machizawa in 2004 aimed to explore the limitations and neural mechanisms underpinning visual working memory. Participants in the study were presented with arrays of colored rectangles and tasked with remembering their colors and locations. Following a brief delay, they were shown a second array and had to determine if it was identical to the first or if one rectangle had changed color. The number of rectangles varied to assess memory capacity. EEG recordings

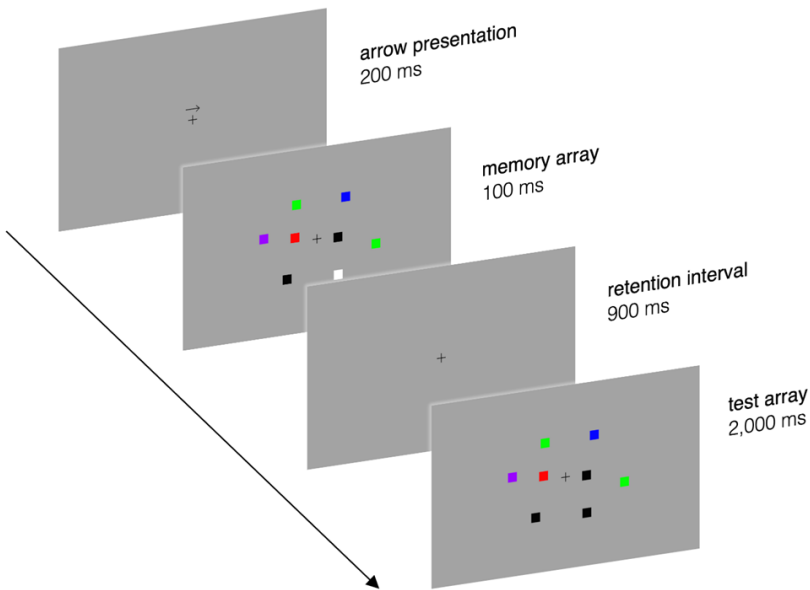


Figure 10.7: Experiment Task

were used to monitor neural activity, particularly focusing on the contralateral delay activity (CDA).

The study found that participants' accuracy in detecting changes declined as the number of items increased, with a notable drop when the set size exceeded three to four items, indicating a memory capacity limit of about 3-4 items.

Correspondingly, the amplitude of the CDA increased with the number of items up to this capacity limit, beyond which it plateaued, suggesting a fixed neural resource for visual working memory. This research highlighted that visual working memory is constrained by a capacity limit and established the CDA as a neural marker for the number of items held in memory, offering significant insights into the cognitive and neural mechanisms of working memory limitations. Once Psychtoolbox is installed, you must run the WorkingMemoryCapacity.m script. The code will first prompt participants to complete an identification form.

```
prompt = {'Participant ID (1 - 999):', ...  
          'Please enter your sex (m/w/d):', ...  
          'Please enter your year of birth:'};
```

This allows experimenters to keep track of the data collected during the experiment. Additionally, the experiment provides options for adjusting specific parameters. You can change the number of squares or objects to remember and the total number of trials, determining how often the task will be repeated. In psychophysics, repeating the task is important because some effects may be too subtle to detect in just a few trials; however, repeating the task allows these effects to become more apparent when averaged over a larger number of trials.

```
% Set number of colored squares per hemifield  
% NOTE: Parameters used by Vogel & Machizawa (2004): 1,  
2, 3, 4, 6, 8, 10  
nSquares = 4;  
  
% Number of trials (excluding practice trials)  
% NOTE: Vogel & Machizawa (2004) conducted 240 trials in  
each experiment  
nTrials = 240;
```

```
% Number of practice trials
```

```
nPracticeTrials = 10;
```

SOA stands for “Stimulus Onset Asynchrony.” It refers to the time interval between one stimulus's onset and another. SOA is commonly used in experimental psychology, particularly in studies investigating perception, attention, and reaction times. By manipulating the SOA, researchers can examine how the timing of stimuli affects cognitive processes and behavioral responses. For example, in a visual attention experiment, varying the SOA between a cue and a target can help determine the speed and efficiency of attentional shifts. In our case, this variable makes the human subject unable to predict when the next stimulus will happen.

```
% Set range to be used for the SOA (values are the ones  
used by Vogel &
```

```
% Machizawa (2004))
```

```
Duration.stimOnsetAsyncMinSecs = 0.3; % in secs
```

```
Duration.stimOnsetAsyncMaxSecs = 0.4; % in secs
```

Some other parameters deal with the timing of the experiment, which is crucial when getting certain results for working memory.

```
% Set remaining timing parameters for the experiment  
(again, values are the
```

```
% ones used by Vogel & Machizawa (2004))
```

```
Duration.arrowSecs = 0.2; % in secs
```

```
Duration.memoryArraySecs = 0.1; % in secs
```

```
Duration.retentionIntervalSecs = 0.9; % in secs
```

```
Duration.testArraySecs = 2; % in secs
```

Maintaining a consistent viewing distance in working memory tasks is crucial for several reasons. Firstly, it ensures that the visual angle of the stimuli remains constant, allowing for uniform perception across trials and participants. This consistency is essential for controlling the perceptual aspects of the task, ensuring that all stimuli appear the same size and are processed

similarly by the visual system. A proper viewing distance also guarantees that stimuli are visible and in focus, preventing blurriness or difficulty distinguishing the items, which could increase cognitive load and lead to errors. Controlling the viewing distance also minimizes the need for large eye movements, reducing variability in how stimuli are processed and remembered. Large eye movements could cause some stimuli to fall outside the central part of the visual field, where visual acuity is highest, thus impairing memory encoding.

Furthermore, a consistent viewing distance helps preserve the spatial relationships between stimuli, which is crucial in tasks where spatial configuration and relative positions are important for performance. Standardizing viewing distance across studies also allows for better comparison of results, enabling researchers to draw broader conclusions about visual working memory. Lastly, it helps control for variations in depth perception, ensuring that all participants experience the stimuli in a similar two-dimensional plane without unintended depth cues. Overall, maintaining an appropriate viewing distance ensures uniform perception, reduces variability, and enhances the reliability and validity of working memory research.

```
% (Orthogonal) distance from eye to screen in mm
% NOTE: This depends heavily on the setup (chair, desk,
laptop vs. external
% monitor, etc.) that's being used. With my setup, I
measured the
% following distances (using a height-adjustable desk
and desk chair that
% are properly adjusted to me):
%   - w/ laptop screen (MacBook Pro 16"): 550 mm
%   - w/ external monitor (Dell U4021QW 40" attached to
Ergotron HX): 650 mm
viewingDistanceMM = 550; % in mm
```

## Visual angle

Another important factor is the size of the objects to be retained in working memory. In this experiment, they subtend a visual angle of 0.65 degrees.

**% NOTE:** Vogel & Machizawa (2004) used squares with a size of 0.65° x 0.65°.

squareSizeVA = 0.65; % in degrees of visual angle

Visual angle measures how large an object appears to an observer based on its size and distance from the observer. It is important in fields like vision science and experimental psychology because it helps quantify how much of the visual field an object occupies. Here's how visual angle is calculated: ### Formula for Visual Angle The visual angle ( $\theta$ ) in degrees can be calculated using the formula:

$$\theta = 2 \times \arctan\left(\frac{d}{2D}\right) \quad (10.1)$$

Where:

- $\theta$  = Visual angle in degrees
- $d$  = Diameter or height of the object (or stimulus)
- $D$  = Distance from the observer to the object Steps for Calculation

1. Measure the Object's Size ( $d$ ): Determine the object's size or stimulus in units such as centimeters or inches.
2. Measure the Viewing Distance ( $D$ ): The distance from the observer's eyes to the object or stimulus. This is often done in centimeters or inches.
3. Apply the Formula: Substitute the values for  $d$  and  $D$  into the formula to find the visual angle.

## ***Example Calculation***

Suppose you have an object 10 cm in diameter (d), viewed from a distance of 100 cm (D).

1. Convert the measurements into the formula:

$$\theta = 2 \times \arctan\left(\frac{10/2}{100}\right) = 2 \times \arctan\left(\frac{5}{100}\right) \quad (10.2)$$

2. Calculate the visual angle:

$$\theta = 2 \times \arctan(0.05) \approx 2 \times 2.86^\circ \approx 5.72^\circ \quad (10.3)$$

So, the visual angle of the object is approximately 5.72 degrees.

## ***Subject responses***

Participants are asked to respond if they notice a change in the square configuration, indicating whether the pattern is identical or different. Psychtoolbox uses specific code to facilitate response mechanisms, such as the keyboard. In this case, pressing the letter 'J' signifies that the pattern is identical while pressing 'F' indicates that it is different.

```
% Set keys
% NOTE: The space bar will be used by participants to
navigate through
% instructions. To indicate a decision, participants
will press either 'J'
% (indicating identical arrays) or 'F' (indicating
different arrays).
% Finally, the escape key can be used to prematurely end
the experiment.
Key.space = KbName('SPACE');
Key.identical = KbName('J');
```

```
Key.different = KbName('F');
Key.escape = KbName('ESCAPE');
```

The response is then logged after every trial of the experiment.

```
% 7.2 Store participant's response
trials.Response(iTrial) = response;
```

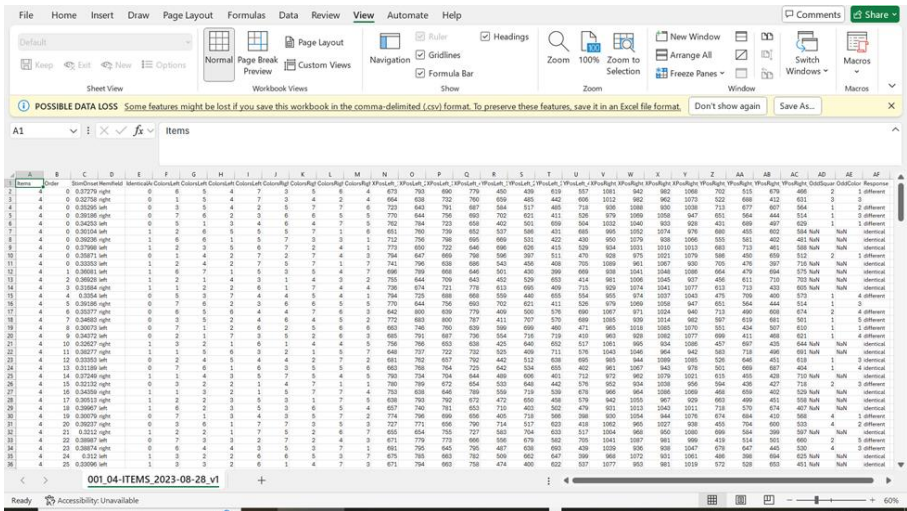


Figure 10.8: Data in Excel File

The responses, along with the data from each trial, are then saved in an Excel file.

The package from Marvin Theiss also includes a procedure for analyzing the data generated from the experiment. This script processes the CSV file created

ParticipantID	Items	Trials	HitRate	FalseAlarmRate	Capacity
1	4	239	0.87395	0.025	3.3958

Figure 10.9: Trial Variables

during the experiment and calculates the hit rate, false alarm rate, and working memory capacity. In working memory tasks, capacity is typically calculated using the measure “K,” which represents the number of items a participant can hold in working memory. This measure is often derived from a change detection task where participants are briefly shown an array of visual stimuli, such as colored rectangles. After a short delay, a second array is presented, and participants must determine if it is the same as the first array or if one item has changed. The number of items in the arrays, or set size, varies across trials. The proportion of correct responses (hit rate) and incorrect responses when no change occurs (false alarm rate) are recorded to calculate K. The formula for calculating working memory capacity is  $K = S \times (H - F)$ , where S is the set size, H is the hit rate, and F is the false alarm rate. For example, with a set size of 4 items, a hit rate of 0.75, and a false alarm rate of 0.20, the capacity K would be  $4 \times (0.75 - 0.20) = 2.24 \times (0.75 - 0.20) = 2.24 \times (0.75 - 0.20) = 2.2$ . This means the participant can accurately maintain and process about 2.2 items in their visual working memory. This calculation is essential for understanding individual differences in cognitive abilities and comparing performance across different populations or experimental conditions.

In our case, the capacity is approximately 3.4, which means that, on average, the participant (us) can hold and accurately maintain about 3.4 items in their visual working memory. This measure indicates the maximum number of items a person can effectively store and manipulate in their mind over a short period.

### ***Implications of a Capacity of 3.4***

6. **High Performance:** A capacity of 3.4 is relatively high, suggesting that participants can retain and process visual information.
7. **Comparison to Typical Capacities:** This value is above the commonly cited average working memory capacity of 3-4 items, indicating that participants perform at or slightly above average regarding their visual working memory abilities.

8. **Experimental Context:** This capacity is context-dependent and can be influenced by various factors, such as the stimuli's nature, the retention interval's duration, and the specific task demands.
9. **Cognitive Implications:** Higher working memory capacity is often associated with better performance in tasks that require attention, problem-solving, and learning. It suggests that participants can efficiently manage and utilize multiple visual information simultaneously. A working memory capacity of approximately 3.4 means that participants can simultaneously hold and accurately recall around 3.4 visual items, reflecting a robust capacity for visual information processing. This measure provides a valuable understanding of their cognitive abilities and can inform further research or practical applications where working memory plays a crucial role. The most common capacity for visual working memory, often cited in psychological and cognitive neuroscience research, is typically around 3-4 items. This estimate is based on numerous studies investigating the limits of working memory using various tasks and methodologies.

### ***Evidence about capacity (K)***

10. **Classic Studies:** Early research by George Miller in 1956 suggested that the average capacity of short-term memory is about  $7 \pm 2$  items. However, more recent studies focusing specifically on visual working memory have found that this capacity is smaller, generally around 3-4 items.
11. **Empirical Findings:** Many experiments using change detection tasks, similar to the ones described by *Vogel and Machizawa (2004)*, consistently find that participants can hold approximately 3-4 items in visual working memory before their performance declines.
12. **Contralateral Delay Activity (CDA):** Research using neural measures such as CDA supports this capacity limit. The CDA amplitude increases with the number of items held in memory up to about 3-4 items, after which it plateaus, indicating a maximum capacity.

**We invite you to complete this task to determine your working memory capacity.**

## *Acknowledgments*

- The experiment code is based on the Psychtoolbox library. For more information about Psychtoolbox, visit Psychtoolbox.
- The grammarly.com Grammar Checker was used to check written text for spelling and grammar mistakes.
- Screenshots and screen capture videos were taken/recorded using macOS' built-in Screenshot app.
- The Gifski app was used to convert screen capture videos into GIFs.





## **Chapter 11**

# **Tuning In: Exploring the Marvels of The Auditory System**

# Introduction to the Auditory System

The auditory system is one of the most remarkable and specialized sensory systems in the human body, playing a crucial role in our ability to interact with the world. This system is responsible for detecting, transmitting, and processing sound, allowing us to experience a vast array of acoustic stimuli—ranging from the rumbling of thunder and the roar of a crowd to the subtle rustling of leaves and the intricate harmonies of a symphony. The auditory system's ability to discern these diverse sounds with incredible precision is essential for communication, environmental awareness, and the appreciation of music and language. The auditory system is a complex network that begins with the ear's anatomy and extends to the intricate pathways within the brain. In addition to the natural hearing processes, this chapter will explore the role of auditory nerves and how they connect the ear to the brain, forming the pathways that carry sound information.

Furthermore, we will examine the function of hearing assistance technologies, such as hearing aids and cochlear implants, designed to support individuals with hearing impairments. These technologies have advanced significantly over the years, offering new possibilities for those who experience hearing loss, helping to restore the ability to perceive and enjoy the rich world of sound. By understanding how this system operates, we gain insights into the marvels of human hearing and how technology can enhance it for those in need. By the end of this chapter, you will be able to:

1. *Understand the in-depth anatomy of the ear and the mechanism of hearing.*
2. *Identify the importance of the auditory nerves and their role in hearing.*
3. *Understand the different forms of hearing loss and their various impacts on the auditory system.*
4. *Explain the principles behind hearing assistance techniques such as cochlear implants.*

# Overview of Auditory System Function

The auditory system's primary function is to convert sound waves into electrical signals for our brain to interpret. Besides simply detecting sound, the auditory system also interprets the various characteristics of sound, such as pitch, loudness, and timbre. The overall system of hearing is accomplished through several steps: the outer ear collects sound waves, which travel through the middle ear via mechanical vibrations; the inner ear transforms sound waves into fluid waves, and the brain generates neural signals. The anatomy of each ear component and how they collectively achieve this function will be explored in detail in this chapter. Additionally, complex signal transmissions, processing, and interpretation in the brain will be discussed in detail.

## The Ear Anatomy

The human ear is an intricate and highly specialized organ responsible for the critical sense of hearing. It is divided into three main sections: the outer ear, middle ear, and inner ear. Each section plays a distinct and vital role in converting sound waves from the environment into electrical signals that the brain can interpret as sound. The seamless cooperation between these sections allows us to perceive a wide range of sounds, from the faintest whisper to the loudest explosion. The basic structure of the human ear is shown in Fig. 11.1 [231].

### *Outer, Middle, and Inner Ear Anatomy*

#### *Outer Ear*

The outer ear serves as the gateway to the auditory system, capturing sound waves and funneling them toward the deeper structures of the ear. It comprises two primary components: the auricle (or pinna) and the external auditory meatus (ear canal). The auricle, the visible part of the ear, is uniquely shaped to help gather sound waves from the environment and direct them into the ear canal. Its curved, cartilaginous structure enhances our ability to detect the direction from which sounds are coming, a crucial aspect of spatial awareness. The external auditory meatus is a narrow passageway lined with skin, hair, and glands that produce earwax, which helps protect the ear by trapping dust and

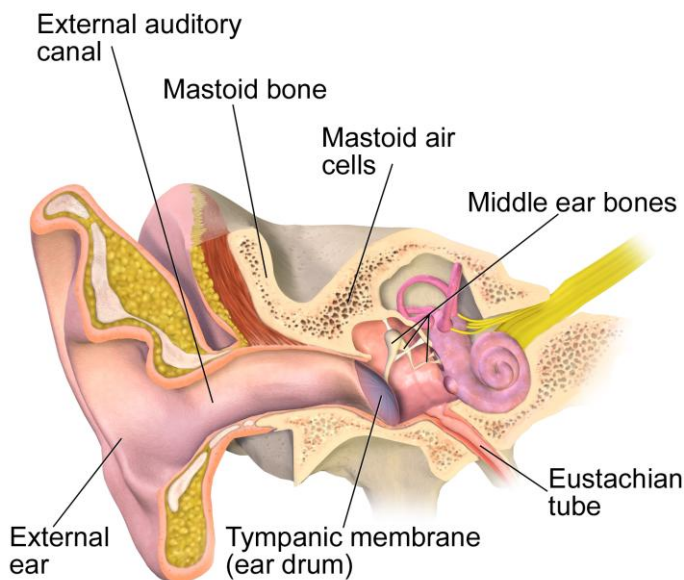


Figure 11.1: The structure of the human ear [231]

other foreign particles. The outer ear's primary function is to collect and direct sound waves to the tympanic membrane, or eardrum, which marks the boundary between the outer and middle ear. The tympanic membrane is a thin, cone-shaped membrane that vibrates in response to incoming sound waves, initiating the process of sound transmission deeper into the ear.

### ***Middle Ear***

The middle ear is an air-filled cavity located behind the eardrum. It plays a critical role in amplifying and transmitting sound vibrations from the outer ear to the inner ear. The middle ear contains three tiny bones known as the ossicles: the malleus (hammer), incus (anvil), and stapes (stirrup). These bones are the smallest in the human body, yet they are essential for hearing. When sound waves cause the tympanic membrane to vibrate, these vibrations are

# The Internal Ear

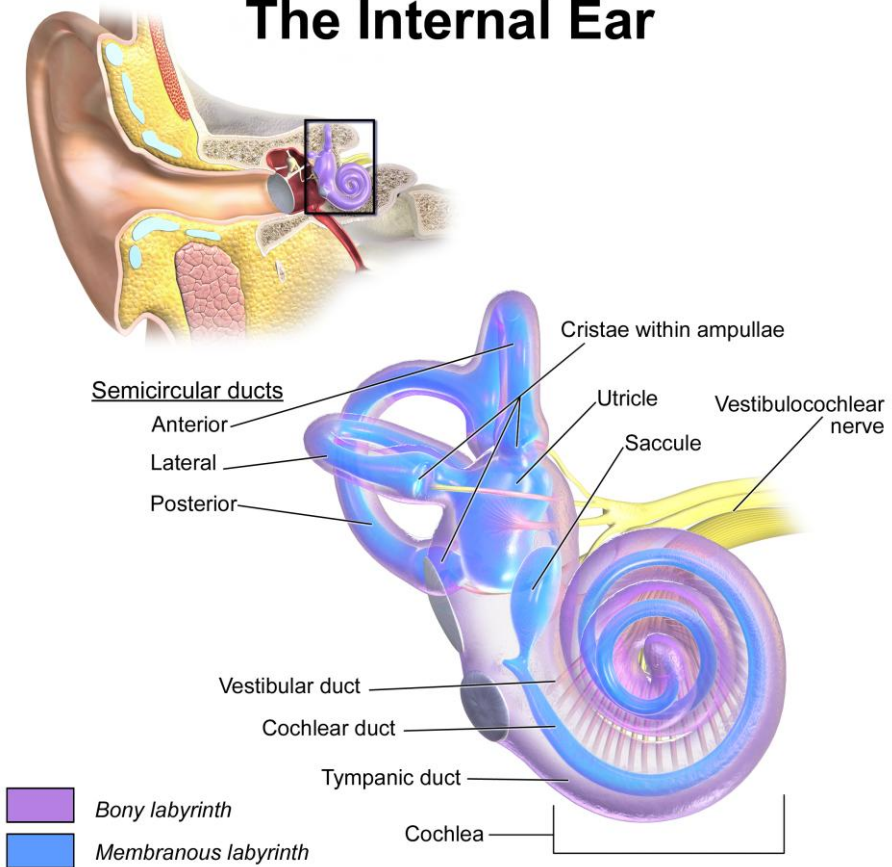


Figure 11.2: The Inner Ear [232]

transferred to the malleus, which is attached to the eardrum. The malleus then transmits the vibrations to the incus, which, in turn, passes them to the stapes. The stapes, the final bone in the chain, are connected to the oval window, a membrane-covered opening that leads to the inner ear.

The primary function of the ossicles is to amplify the sound vibrations. As the vibrations pass through the ossicles, they are concentrated and strengthened to overcome the impedance mismatch between the air-filled middle ear and the fluid-filled inner ear. This amplification ensures sound waves are efficiently

transmitted into the cochlear fluid. The Eustachian tube connects the middle ear to the nasopharynx (upper part of the throat). This small canal helps equalize air pressure on both sides of the eardrum. This equalization is important for maintaining proper ear function and preventing discomfort during activities such as swallowing, yawning, or changes in altitude.

### ***Inner Ear***

The inner ear is a complex and highly sensitive structure responsible for hearing and balance. It contains two main components: the cochlea, which is responsible for listening, and the vestibular system, which is responsible for balance. The general inner ear anatomy is shown in Fig. 11.2 [232]. The cochlea is a spiral-shaped, fluid-filled organ that resembles a snail shell. It is the primary organ of hearing, where mechanical sound vibrations are transformed into electrical signals that the brain can interpret. The cochlea is divided into three fluid-filled compartments: the scala vestibuli, scala media, and scala tympani. The scala vestibuli and scala tympani contain perilymph, similar to cerebrospinal fluid. In contrast, the scala media contains endolymph, a fluid with a unique ionic composition essential for hair cell function.

At the heart of the cochlea lies the basilar membrane, a flexible structure that runs along the length of the cochlea and plays a key role in sound processing. Embedded within the basilar membrane are thousands of tiny hair cells, which are the sensory receptors of the auditory system. As sound vibrations travel through the fluid in the cochlea, they cause specific regions of the basilar membrane to vibrate. Different sound frequencies stimulate various areas of the basilar membrane, with high-frequency sounds affecting the base of the cochlea and low-frequency sounds affecting the apex. The basilar membrane movement causes the hair cells to bend, triggering the conversion of mechanical energy into electrical impulses. These impulses are then transmitted to the brain via the auditory nerve, where they are interpreted as sound.

Although this chapter focuses primarily on the auditory system, it is important to briefly mention the vestibular system, which is also housed within the inner ear. The vestibular system comprises the semicircular canals and otolithic organs, which detect changes in head position and motion. This system plays

a crucial role in maintaining balance and spatial orientation. While not covered in detail here, the vestibular system's role in balance and coordination is essential for overall sensory integration.

## **Sound Characteristics**

Now that you have a general understanding of the anatomy of the ear and a brief description of how hearing works let's discuss in greater detail the mechanism of how sound waves are transmitted to the brain in the form of speech or music for us to hear. First, we need to understand sound waves and the properties of sound that our anatomy allows us to discern. Several physical properties characterize sound, such as frequency, amplitude, and timbre.

### ***Frequency***

The frequency of a sound wave is usually measured in cycles per second or Hertz. A frequency of 1 Hz indicates one complete sound wave cycle per second; this may also be called an oscillation. The frequency is directly related to the perceived pitch. Higher frequencies correspond to higher pitches. The human auditory system can detect sounds from approximately 20 Hz to 20,000 Hz, although our sensitivity is highest between 500 Hz and 5,000 Hz. A graph of a sine wave showing a constant frequency and amplitude is shown in Fig. 3. In this image, if the frequency, or the number of oscillations, increased, this would be perceived as a higher pitch sound. If it decreased, it would be perceived as a lower pitch sound.

### ***Amplitude***

The amplitude of a sound wave is measured in decibels (dB). We perceive amplitude as loudness. In a sound wave, the amplitude is the wave's height, where larger amplitudes produce louder sounds. In Fig. 3, if the amplitude increased in height, the sound would be more intense.

### ***Timbre***

Timbre refers to a sound's quality; this enables us to distinguish between different sound sources. For example, when a musician plays the violin with a singer, our ear can discriminate the violin sound and identify its source from the singer, even when both sounds are produced at the same pitch and loudness.

This is arguably one of the more fascinating concepts of human hearing and is essential for identifying complex sounds.

## Mechanism of Hearing

We can explore the hearing mechanism in more detail with a fundamental understanding of sound waves and auditory system anatomy. Sound waves enter the ear canal and cause the eardrum to vibrate—the ossicles transmit and amplify vibrations. The ossicles enable proper transmission of sound waves to vibrations of the cochlear fluid by impedance matching [233]. Additionally, these ossicles focus sound on a concentrated area of the cochlea, the oval window. When the cochlear fluid waves move, the basilar membrane also moves. The projections of the inner hairs, called stereocilia, are sensitive to the movement of the basilar membrane. This movement of the basilar membrane bends the stereocilia, which causes the opening of ion channels and depolarization, converting the fluid wave into an electrical signal. The outer hairs of the basilar membrane also change in size, which amplifies and fine-tunes the cochlea's response.

The basilar membrane is sensitive to various frequencies and will respond differently along its length to each frequency. The base of the cochlea is stiffer, narrower, and more sensitive to high-frequency sounds. The apex of the

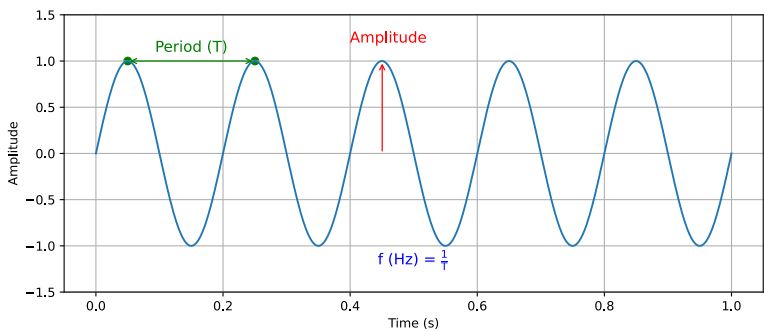


Figure 11.3 An example sine wave demonstrating amplitude and frequency.

membrane is wider, more flexible, and more sensitive to low-frequency sounds. This varied sensitivity to different sound frequencies is referred to as tonotopic organization. Specific nerve endings positioned along the basilar membrane enable us to distinguish the magnitude and range of frequencies, up to around 20,000 Hertz (Hz) [234].

## **Auditory Nerves and Processing**

The vestibulocochlear nerve, or cranial nerve 8, is responsible for the ability to hear and balance. The cochlear nerve component transmits the electrical signals from the cochlea to the brain for sound to be processed and interpreted. As many as 30,000 auditory nerve fibers comprise our vestibulocochlear nerve [235, p. 9]. This allows us to discern the range of piano notes and voices we can hear. As we will discuss later, damage to this nerve can significantly impact our auditory processing.

### ***Cochlear Nuclei***

The electrical impulses from the auditory nerves are sent to the cochlear nuclei, which are in the rhomboid fossa of the brainstem. The cochlear nuclei are the first major relay station where signals are refined. Here, sound information is split into parallel processing streams that separately handle different features of the sound, such as pitch, timing, and intensity. The dorsal cochlear nucleus (DCN) integrates auditory signals with other sensory inputs, crucial for understanding sound in a noisy environment. In contrast, the ventral cochlear nucleus (VCN) processes the timing and intensity of sound with high precision, allowing for the accurate localization of sound sources.

### ***Superior Olivary Complex***

As the auditory signals travel upward from the cochlear nuclei, they reach the Superior Olivary Complex (SOC) in the brainstem's pons. The SOC is crucial for binaural hearing. This is the process where our brain uses input from both ears to determine the location of a sound source. The SOC is in the first place in the auditory pathway, where information from both ears converges. Auditory signals from the right ear crossover are forwarded to the contralateral side of the brain; however, some research suggests that ipsilateral signals also play

a significant role [236]. The collection of steps before the brainstem is considered the peripheral auditory system, and the brain stem and the brain are the central auditory nervous system.

### ***Inferior Colliculus***

The auditory signals are relayed from the SOC to the inferior colliculus. The inferior colliculus is a pair of major integration centers for auditory information. It receives inputs not only from the SOC and cochlear nuclei but also directly from the auditory cortex. The inferior colliculus is responsible for further refining sound processing handling complex aspects such as temporal patterns, spatial location, and specific pitch and intensity modulation features. This area acts as a filter and relay station, ensuring that only important auditory information is transmitted to the higher brain centers.

### ***Medial Geniculate Nucleus***

The information from the inferior colliculus is then sent to the thalamus, specifically the medial geniculate nucleus of the thalamus. The medial geniculate nucleus has several subnuclei that play a role in processing auditory information. Its primary function is to act as the main relay from the inferior colliculus to the auditory cortex, A1, located in the temporal lobe.

### ***Temporal Lobe***

#### ***Primary Auditory Cortex***

This primary auditory cortex (A1) and the associative or secondary cortex are collectively called Heschl's gyrus. Fig. 11.4 shows the approximate



Figure 11.4 An AI generated image of the brain with the approximate area of the primary auditory cortex shaded in red.

location of the primary auditory cortex. The primary auditory cortex is the first cortical area to receive auditory input and is responsible for the basic interpretation of the auditory signals. Here, the auditory information is mapped tonotopically, with different regions of the auditory cortex responding to other frequencies. This highly precise tonotopic organization allows for the detailed frequency discrimination we discussed earlier. This is fundamental to perceiving speech, music, and other complex sounds.

In addition to frequency mapping, the auditory cortex is involved in the initial stages of sound processing, such as detecting the presence of a sound, determining its pitch, and spatial location. These basic processing tasks proceed to the more complex auditory processing by the associative cortex.

### ***Secondary Auditory Cortex***

The secondary auditory cortex (A2) lies adjacent to A1 in the temporal lobe and is critical in higher-order sound processing. This region begins to interpret complex auditory signals, such as recognizing speech or music and distinguishing different types of sounds. Two primary streams are within the secondary cortex: the ventral and dorsal pathways. The ventral pathway plays a significant role in sound identification and recognition. The dorsal pathway is involved in spatial localization of sounds.

### ***Wernicke's Area***

Wernicke's area is within the temporal lobe. This site is responsible for our higher-order speech comprehension. Wernicke's area plays a vital role in processing the meaning of spoken and written language. Essentially, this area links the sound of words to their associated meanings. Disruptions to this area can result in Wernicke's aphasia, severely impairing speech comprehension. Interestingly, speech production itself can remain unaffected.

## **Hearing Loss**

There are three major types of hearing loss: conductive, sensorineural, and mixed [237]. These three types of hearing loss affect the auditory systems differently and have distinct pathophysiology. The next sections will discuss treatment methods for each type of hearing loss.

### ***Conductive Hearing Loss***

Conductive hearing loss occurs when there is an issue with conducting sound waves. Therefore, this hearing loss primarily affects the outer and middle ears. Some common causes of conductive hearing loss include structural abnormalities or trauma to the eardrum, ear infections, objects, and fluid. These problems prevent sound from being transferred from the outer and middle ear to the inner ear.

### ***Sensorineural Hearing Loss***

Where conductive hearing loss encompasses problems with the outer and middle ears, sensorineural hearing loss occurs with issues with the inner ear. This hearing loss occurs when problems with the cochlea or auditory nerves lead to the brain. It is the most common type of hearing loss and is usually permanent. Some examples of sensorineural hearing loss include aging, loud noise exposure, and illnesses. Age-related hearing loss is specifically referred to as presbycusis.

### ***Mixed Hearing Loss***

Mixed hearing loss includes a combination of conductive and sensorineural loss. This means there is damage to both the outer/middle and inner ear. For example, say you had an ear infection followed by extremely loud noise exposure. These two combined issues lead to mixed hearing loss and are the most difficult to address.

### ***Genetic Factors***

Genetic mutations can play a role in congenital and progressive hearing loss like those discussed above. Mutations of specific genes can cause sensorineural hearing loss. Recent advances in genetic testing show promise for targeted interventions for individuals with these genetic mutations.

### ***Trauma-Induced Hearing Loss***

Although traumatic incidents may still fall under the scope of conductive, sensorineural, or mixed hearing loss, they deserve discussion. Various types of

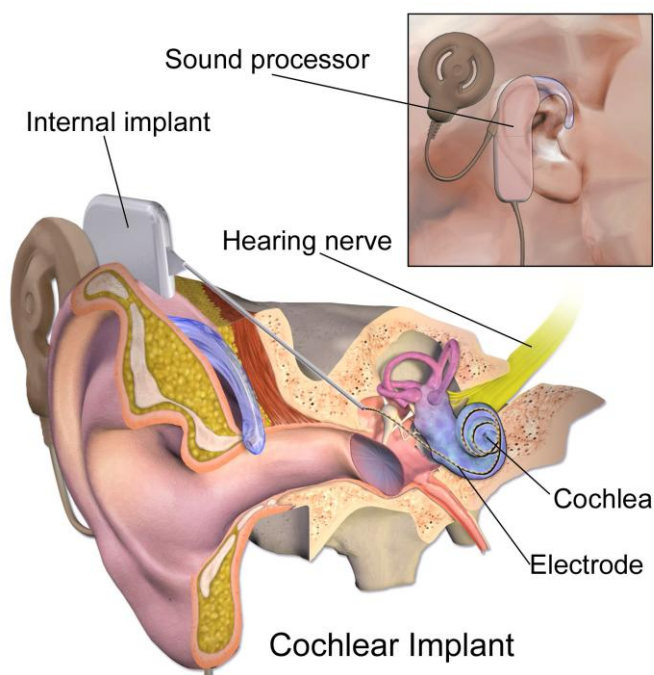


Figure 11.5: Image of an ear with cochlear implant [238]

trauma can influence the method and magnitude of the subsequent hearing loss. Traumatic brain injury, for example, may lead to disturbance of the auditory cortex. Damage to this region or the surrounding area can range from buzzing and roaring sensations to complete deafness. Earlier in this chapter, we briefly discussed Wernicke’s aphasia, a specific type of traumatic-induced hearing loss disorder. A different kind of traumatic-induced hearing loss includes noise-induced hearing loss. This sensorineural hearing loss can be caused by prolonged exposure to loud noise or sudden, damaging acoustic trauma. Direct trauma to the eardrum in the form of punctures will also contribute to hearing loss. There are various degrees to which trauma-induced hearing loss can be treated or mitigated.

# Hearing Loss Treatment

## *Hearing Aids*

Hearing aids are small electronic devices designed to assist individuals with hearing loss by amplifying sounds. These devices are particularly beneficial for those experiencing mild to moderate hearing loss, whether due to conductive issues, such as blockages or damage in the outer or middle ear, or sensorineural problems, such as damage to the inner ear or auditory nerve. The basic components of a hearing aid include a microphone, amplifier, and speaker. The microphone picks up sound from the environment, which is then converted into electrical signals. The built-in amplifier increases the strength of these signals, making them louder and easier to hear. Finally, the amplified signals are delivered to the ear through a speaker.

Modern hearing aids are highly sophisticated, offering a range of customizable features that allow them to be precisely tuned to the user's specific hearing profile. This customization is crucial because hearing loss often affects different frequencies unevenly. For example, some individuals may have difficulty hearing high-pitched sounds, while others may struggle with low-frequency noises. Advanced hearing aids can be programmed to amplify specific frequencies more than others, thereby providing a tailored listening experience that enhances speech comprehension and reduces background noise. Additionally, modern hearing aids often include directional microphones, noise reduction, and wireless connectivity to smartphones and other devices, making them versatile tools for managing hearing loss in various environments.

## *Cochlear Implants*

Cochlear implants represent a more advanced technological solution for individuals with severe to profound sensorineural hearing loss, typically resulting from damage to the hair cells within the cochlea; unlike hearing aids, which amplify sound, cochlear implants work by directly stimulating the auditory nerve, bypassing the damaged parts of the ear. This approach enables individuals who might otherwise be unable to hear to regain a degree of auditory perception.

The cochlear implant system consists of both external and internal components. The external part, usually worn behind the ear, includes a microphone and sound processor that captures and converts sound into digital signals. These signals are then transmitted to a receiver implanted under the skin behind the ear. The internal receiver sends the signals to a series of electrodes surgically implanted into the cochlea. These electrodes directly stimulate the auditory nerve fibers, allowing the brain to perceive sound. While cochlear implants do not restore normal hearing, they can significantly improve speech understanding and environmental awareness, enabling users to participate more fully in everyday activities. Fig. 11.5 [238] shows a diagram of what a cochlear implant can look like.

### ***Ethical Considerations of Auditory Treatments***

While cochlear implants offer life-changing benefits for many individuals, their use also raises several ethical considerations, particularly within the Deaf community. For some, auditory treatments are seen as a medical miracle that can restore a sense of hearing to those who have lost it. However, others argue that auditory treatments represent an attempt to "fix" deafness, which they view not as a disability but as a unique cultural identity. This perspective is particularly strong within the Deaf community, where sign language is celebrated as a rich and fully developed means of communication, and Deaf culture is embraced as a valuable and distinct way of life.

One of the primary ethical concerns centers around using auditory treatments in young children, especially infants who have not yet developed language or cultural identity. Parents and medical professionals often advocate for early implantation to maximize the potential for the child to develop spoken language skills. However, others argue that this decision may impose a hearing-centric view on the child before they are old enough to choose their identity and communication preferences. Another ethical consideration involves the potential impact on the Deaf community. As more individuals opt for auditory treatments, there is concern that Deaf culture and sign language may be marginalized or devalued. Advocates for Deaf culture emphasize the importance of preserving and promoting sign language as a legitimate and vital

means of communication, regardless of whether an individual has a cochlear implant.

There is also the question of access and equity. Auditory treatments are expensive and require significant follow-up care, including speech therapy and regular adjustments to the device. This can create disparities in access, with only those with sufficient financial resources or healthcare coverage benefitting from the technology. Additionally, the long-term success of auditory treatments depends on consistent and intensive auditory training, which may not be available to all recipients, particularly in low-resource settings.

In conclusion, while auditory treatments have the potential to significantly improve the quality of life for individuals with severe hearing loss, they also bring to light important ethical questions about identity, culture, access, and the definition of disability. Individuals, families, and healthcare providers must carefully weigh these considerations when making decisions about cochlear implantation.

## **Neuroengineering Applications**

Neuroengineering has paved the way for innovative approaches to auditory rehabilitation. The previous fundamentals discussed in this chapter are essential for any engineer looking to further these treatments and technologies. As these technologies advance, so does our understanding of the auditory system. The development of cochlear implants and hearing aids has tremendously impacted those with hearing loss. Current research explores how to enhance these treatments to target other pathways and improve sound quality and speech recognition, especially in noisy environments. Research methods utilizing MATLAB and Psychtoolbox enable the accessibility of this type of research to many researchers of various experience levels.

### ***MATLAB and Psychtoolbox***

As you have seen from the previous sections in this chapter, MATLAB is a powerful tool for conducting various experiments and data processing. Psychophysics Toolbox, also known as Psychtoolbox, is a popular suite of

functions for MATLAB and can perform auditory and visual experiments [239]. The ease of use of this tool within MATLAB provides a vast array of simulation, analysis, and experimental design applications that can be used to conduct research in the auditory system.

### ***Other Experimental Methods***

Aside from the applications of MATLAB and Psychtoolbox, commercial-grade techniques such as the auditory brainstem response (ABR) and otoacoustic emissions tests (OAE) are frequently used in medical applications to screen for hearing loss. The OAE test can measure the response of the cochlea through auditory stimulation. The ABR test utilizes the principles of EEG that you learned earlier in this text and involves measuring the brain's electrical activity in response to sound stimuli.

## **Chapter 11: Summary**

The auditory system is very complex, enabling us to perceive and interpret the sounds around us. Understanding the anatomy, function, and pathophysiology is important for neuroengineers. Advances in hearing loss treatments, such as hearing aids and cochlear implants, are made possible by the research conducted in neuroengineering. Using the information presented in this chapter and the preceding chapters, you are armed with the knowledge to understand and conduct your research that can progress future technology and treatments.



# Chapter 11: Learning Activities

## Learning Activity 11.1

### *Connecting Chaos Theory and Cochlear Prostheses through a Mind Map*



#### ***Objective***

Students will independently explore the relationship between chaos theory and cochlear prostheses by creating a mind map, fostering an understanding of complex systems and their applications in medical technology.

#### ***Materials Needed***

- Large sheets of paper or whiteboards
- Markers or pens
- Reference materials on chaos theory and cochlear prostheses (e.g., textbooks, articles, diagrams)

#### ***Activity Outline***

- 1. Introduction (10 minutes)**
  - Provide a brief overview of chaos theory, explaining its principles and significance in understanding complex, dynamic systems.
  - Introduce cochlear prostheses, describing their function, components, and role in aiding individuals with hearing loss.
  - Explain the purpose of the activity: to draw connections between the seemingly disparate concepts of chaos theory and cochlear prostheses through a mind map.
- 2. Individual Mind Map Creation (30 minutes)**
  - Each student will create a mind map on a large sheet of paper or whiteboard.
  - They should place "Chaos Theory" and "Cochlear Prostheses" as the central nodes and branch out from these nodes to explore subtopics and connections.
  - Encourage students to think creatively about how principles of chaos theory (such as sensitivity to initial conditions, nonlinearity, and complex, unpredictable behavior) might

relate to the design, functionality, or performance of cochlear prostheses.

- Students should also consider how cochlear prostheses operate within the complex environment of the human auditory system, which can exhibit chaotic properties.

**3. Reflection and Note-Taking (10 minutes)**

- After completing their mind maps, students should reflect on their work and take notes on the following:
  - Key connections they identified between chaos theory and cochlear prostheses.
  - Any challenges they faced while drawing the mind map and how they overcame them.
  - Insights or new understandings they gained through the activity.

**4. Class Discussion and Reporting (10 minutes)**

- Each student will present their mind map to the class, explaining the connections they identified and the reasoning behind them.
- After each presentation, allow time for questions and comments from the class to foster a deeper understanding and exploration of the topic.

**5. Conclusion (5 minutes)**

- Summarize the key points discussed during the class presentations, highlighting any particularly insightful or unique connections made.
- Discuss the broader implications of applying chaos theory to understanding and improving medical technologies like cochlear prostheses.
- Encourage students to continue exploring interdisciplinary connections in other areas of science and technology.

***Assessment:***

- **Participation:** Ensure that each student actively participates in the mind map creation and class discussion.
- **Creativity and Depth:** Evaluate each student's mind map for creativity, depth of thought, and the ability to draw meaningful connections between chaos theory and cochlear prostheses.

- **Presentation:** Assess each student's presentation for clarity, coherence, and engagement with the class.

### ***Follow-Up:***

- Assign a research project where students investigate another medical technology through chaos theory, creating a detailed report or presentation on their findings.
  - Plan a guest lecture or webinar with a professional in biomedical engineering or applied mathematics to provide real-world insights into the connections between chaos theory and medical technologies.
- 

## **Learning Activity 11.2**

### ***Final Activity: Creating a Concept Map of Book Concepts***

#### ***Objective***

Students will consolidate their understanding of all the concepts covered in the book by creating a comprehensive concept map illustrating how these concepts are interconnected.

#### ***Materials Needed***

- Large sheets of paper or whiteboards
- Markers or pens
- Sticky notes (optional)
- Reference materials, including notes, textbooks, and previous assignments

#### ***Activity Outline***

1. Introduction (5 minutes)



- Explain the purpose of the activity: to create a concept map that connects all the concepts covered in the book to date.
  - Emphasize the importance of understanding the relationships between different concepts for a holistic understanding of the subject matter.
2. **Preparation (10 minutes)**
    - Allow students to gather their notes, textbooks, and other reference materials.
    - Briefly review key concepts covered in the book, providing a list or a quick overview if necessary.
  1. **Creating the Concept Map (30 minutes)**
    - Each student will create a concept map on a large sheet of paper or whiteboard.
    - Students should start by placing the main theme or title of the book at the center of their map.
    - From the central theme, students will branch out to include all major concepts, sub-concepts, and details. Encourage them to use connecting lines, arrows, and labels to show relationships and dependencies between concepts.
    - Students can use different colors or symbols to categorize different types of concepts or to highlight particularly important connections.
    - Sticky notes can be used for ideas that might need rearranging as the map develops.
  2. **Reflection and Note-Taking (5 minutes)**
    - After completing their concept maps, students should reflect on their work and take notes on the following:
      - Key insights gained from creating the map.
      - Any connections between concepts that were previously unclear but became apparent during the mapping process.
      - Areas where they feel they need further review or understanding.
  3. **Class Discussion and Reporting (20 minutes)**

- Each student will present their concept map to the class, explaining the connections they identified and the overall structure of their map.
  - After each presentation, allow time for questions and comments from the class. This will help reinforce the material and provide different perspectives on connecting concepts.
4. **Conclusion (5 minutes)**
- Summarize the key points discussed during the class presentations.
  - Highlight common themes and unique insights from the concept maps.
  - Discuss the value of creating concept maps for understanding and retaining complex information.
  - Encourage students to use concept maps as a study tool in future learning. Learning activity 11.3.Learning activity 11.3

## Learning Activity 11.3

### *Summary Activity: Storytelling to Connect Three Chapters*

#### **Objective**

Students will synthesize and integrate concepts from three book chapters by crafting a compelling and engaging original story, which they can present individually or in teams.

#### **Materials Needed**

- Paper and pens/pencils
- Computers or tablets for writing and research (optional)
- Reference materials, including notes, textbooks, and previous assignments

#### **Activity Outline**

1. Introduction (5 minutes)



- Explain the purpose of the activity: to create a compelling and engaging story that connects concepts from three chapters of the book.
  - Emphasize the importance of creativity and storytelling in understanding and integrating complex ideas.
1. **Selection of Chapters (5 minutes)**
    - Have students, individually or in teams, select three chapters from the book that they will connect through their story.
    - Encourage them to choose chapters with distinct but potentially related concepts to create an interesting narrative.
  2. **Brainstorming and Planning (10 minutes)**
    - Students will brainstorm ideas for their story, thinking about how the concepts from the selected chapters can be interwoven into a cohesive narrative.
    - They should plan the basic outline of their story, including characters, setting, plot, and how the key concepts will be integrated.
  3. **Story Writing (30 minutes)**
    - Students will write their story, ensuring it includes clear connections to the three selected chapters.
    - Encourage creativity and originality, and remind students to make their stories engaging and compelling.
    - Teams can divide writing tasks among members but should ensure the final story is cohesive.
  4. **Reflection and Note-Taking (5 minutes)**
    - After completing their story, students should reflect on their work and take notes on the following:
      - How did they integrate the concepts from the three chapters into their story?
      - Any challenges they faced during the storytelling process and how they overcame them.
      - Insights or new understandings they gained about the chapters through storytelling.
  5. **Class Presentation and Discussion (25 minutes)**
    - Each individual or team will present their story to the class, explaining how it connects the three chapters and the concepts within them.

- After each presentation, allow time for questions and comments from the class to foster a deeper understanding and appreciation of the creative connections made.
6. **Conclusion (5 minutes)**
- Summarize the key points discussed during the class presentations.
  - Highlight particularly creative and effective stories and explain why they stood out.
  - Discuss the value of storytelling in understanding and integrating complex ideas.
  - Encourage students to use storytelling to learn and communicate complex concepts in the future.

## *Assessment*

- **Participation:** Ensure each student actively participates in the story creation and class presentation.
- **Creativity and Engagement:** Evaluate each story for creativity, engagement, and originality.
- **Integration of Concepts:** Assess how well the story integrates and connects the concepts from the three chapters.
- **Presentation:** Evaluate each presentation for clarity, coherence, and engagement with the class.

## *Follow-Up*

Assign a reflective essay where students analyze how storytelling helped them better understand and integrate the material and how they might use this technique in other subjects.

Plan a storytelling workshop where students can practice and refine their storytelling skills, focusing on integrating academic concepts into engaging narratives.



# Chapter 11: Lab introduction

In this series of lab exercises, you will explore auditory perception and the effects of hearing loss using MATLAB. These labs are designed to provide hands-on experience with the Psychophysics Toolbox and MATLAB scripting, enhancing your understanding of auditory system functions and auditory testing methodologies.

In the first lab, you will use MATLAB's Psychophysics Toolbox functions to perform an auditory test. By analyzing the hearing test results of an individual who has undergone tympanoplasty procedures, you will apply your knowledge of the auditory system to identify any abnormal results. This exercise will help you understand how auditory tests are conducted and interpreted in research.

In the second lab, you will simulate hearing loss using MATLAB. You will visualize the results using time-domain plots and frequency spectra by generating sine wave tones at various frequencies and applying a low-pass filter to simulate hearing loss. Additionally, you will listen to the generated tones before and after the simulation to gain an auditory comparison. This lab will provide practical insights into hearing loss's impact on auditory perception.



# Chapter 11: Lab Example 1

## *Overview*

In this chapter, you learned about the Psychophysics Toolbox functions and how they can be used in MATLAB to conduct research. We will utilize one of these Psychtoolbox functions for the laboratory exercise to perform an auditory test. Of note is that the author of this chapter underwent two tympanoplasty procedures to reconstruct both eardrums. This was a result of complications from ear tubes as an infant. Using the knowledge you gained in this chapter and your newfound understanding of the auditory system, try to look for any abnormal results from the MATLAB hearing test performed by the author.

## *Objective*

Use the Psychtoolbox functions in MATLAB to perform a rudimentary hearing test to examine the frequency range you can detect. Plot the frequency range in MATLAB.

## *MATLAB Setup*

First, you should already have MATLAB installed on your computer. Next, go to Psychtoolbox and download the Psychtoolbox files:

<http://psychtoolbox.org/download.html#installation>

Installing Psychtoolbox is straightforward; installation instructions are provided in the link above. After downloading the Psychtoolbox folder, go to it in MATLAB and type “SetupPsychtoolbox” into the MATLAB command line. Done!

## *MATLAB Code*

We will be utilizing the Psychtoolbox function called “ExtendedToneReactionTest()”. This function allows us to generate tones at different frequencies. The code, located on the GitHub link for this chapter, initializes the Psychtoolbox sound driver, generates tones at various



frequencies, plays those frequencies at three-decibel (dB) ranges, and measures response.

**Laboratory Results and Discussion**

Run the code and hit the spacebar (or any key) when you hear a tone. When the author performed this lab, he utilized a high-quality headphone system and listened in a quiet room. However, it should be mentioned that the decibel setting in the code is relative to the computer's volume setting and not reflective of the actual decibel level. Fig. 11.4 shows the test result from the author.

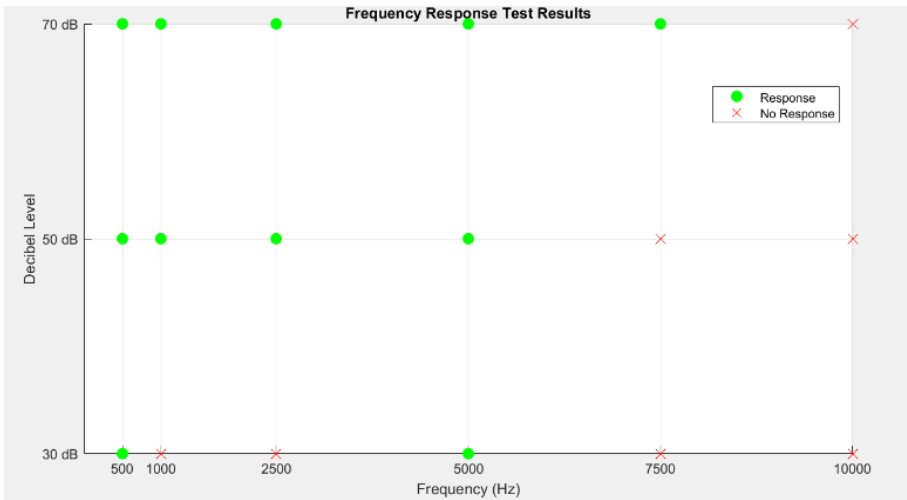


Figure 11.4: Frequency Response Test Results of Male

The green circles on the graph represent a response, and the red x represents no response. Next, let’s observe the results from a healthy adult female volunteer and compare.

If we look at the frequency and decibel response, there is a notable difference in the higher-frequency range. Notice how the author could not hear any 10,000 Hz tones and could only hear the 7,500 Hz tone at 70dB. The female volunteer could listen to both frequencies at 50dB and 70 dB.

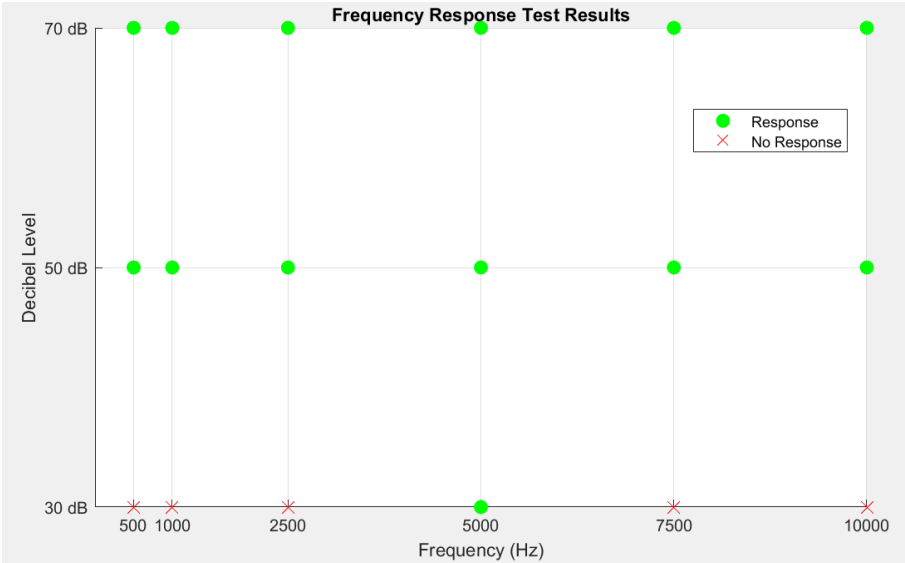


Figure 11.5: Frequency Response Test Results of female volunteer



# Chapter 11: Lab Example 2



## Overview

In this lab, we will be simulating hearing loss using MATLAB. The MATLAB script generates sine wave tones at various frequencies, simulates hearing loss using a low-pass filter, and visualizes the results using time-domain plots and frequency spectra. The script also plays the generated tones before and after simulating hearing loss to provide an auditory comparison.

## Requirements

- MATLAB
- Working speakers
- Audio Toolbox MATLAB
- Signal Processing Toolbox

## Steps

First, you want to navigate to the GitHub page for this textbook. Here is the link

: [https://github.com/bddupre92/Neurobook\\_BME\\_UND](https://github.com/bddupre92/Neurobook_BME_UND)

After you are in Github, navigate to Chapter 11 Lab Example 2, and you will find a MATLAB file named chapter example.m. You will want to open that file in MATLAB and open it as a new script. Look at the code given. Can you recognize any functions you already know of? Do you see some that you don't know? Here is a list of the main functions used in this MATLAB script.

## Main Functions Used

### *sin*

- **Description:** Generates a sine wave.
- **Usage:**  $\text{signal} = 0.5 * \sin(2 * \pi * f * t);$
- **Purpose:** To create the sine wave tones at specified frequencies.

### *butter*

- **Description:** Designs a Butterworth filter.

- **Usage:** `[b, a] = butter(6, cutoff_freq/(fs/2));`
- **Purpose:** To design a low-pass filter to simulate hearing loss.

### *filter*

- **Description:** Applies a digital filter to a signal.
- **Usage:** `signalHearingLoss = filter(b, a, signal);`
- **Purpose:** To apply the low-pass filter to the generated sine waves.

### *sound*

- **Description:** Plays a sound.
- **Usage:** `sound(signal, fs);`
- **Purpose:** To play the generated sine wave tones.

### *pause*

- **Description:** Pauses execution for a specified number of seconds.
- **Usage:** `pause(duration + 0.5);`
- **Purpose:** To allow the sound to finish playing before proceeding.

### *length*

- **Description:** Returns the length of a vector.
- **Usage:** `length(combinedSignal);`
- **Purpose:** To verify the lengths of the combined signals.

### *plot*

- **Description:** Creates a 2D line plot.
- **Usage:** `plot((0:length(combinedSignal)-1)/fs, combinedSignal);`
- **Purpose:** To plot the time-domain waveforms of the signals.

### *fft*

- **Description:** Computes the Fast Fourier Transform (FFT).
- **Usage:** `fftCombinedSignal = fft(combinedSignal);`
- **Purpose:** To compute the frequency spectrum of the signals.

### *abs*

- **Description:** Returns the absolute value.
- **Usage:** `amplitude = abs(fftCombinedSignal)/N;`
- **Purpose:** To compute the magnitude of the FFT.

### *xlim*

- **Description:** Sets the x-axis limits for the current axes.
- **Usage:** `xlim([0, max(frequencies)*1.2]);`
- **Purpose:** To limit the x-axis to the relevant frequency range.

### *xlabel, ylabel, title*

- **Description:** Labels the x-axis, y-axis and sets the plot's title.
- **Usage:** `xlabel('Time (s)'), ylabel('Amplitude'), title('Time-Domain Waveform of Combined Signal (Normal Hearing)');`
- **Purpose:** To add labels and titles to the plots.

### *subplot*

- **Description:** Creates axes in tiled positions.
- **Usage:** `subplot(2, 1, 1);`
- **Purpose:** To create multiple plots in a single figure.

### *disp*

- **Description:** Displays text or variables.
- **Usage:** `disp('Length of combinedSignal:');`
- **Purpose:** To display messages and values in the command window.

This script has four main steps that generate sounds at different frequencies, and then a low pass filter is used to model how hearing loss affects our ability to hear those sounds.

The script then plots time domain signals and a composite frequency spectrum and combines them with the hearing loss signals to compare them. Finally, you will hear what the sounds would sound like for someone experiencing hearing loss. Here's how the script does this.

## ***Step 1: Generate Sounds at Different Frequencies***

### ***Description***

This step generates sine wave tones at specified frequencies and applies a low-pass filter to simulate hearing loss. The original and filtered signals are combined and played.

### ***Functions Used:***

1. **sin:** Generates the sine wave tones.

- `signal = 0.5 * sin(2 * pi * f * t);`
- 2. **butter**: Designs a Butterworth low-pass filter.
  - `[b, a] = butter(6, cutoff_freq/(fs/2));`
- 3. **Filter**: The **low-pass filter is applied** to the generated sine waves.
  - `signalHearingLoss = filter(b, a, signal);`
- 4. **sound**: Plays the generated sine wave tones.
  - `sound(signal, fs);`
- 5. **pause**: Pauses execution to allow the sound to finish playing.
  - `pause(duration + 0.5);`

## ***Step 2: Plot Time-Domain Signals***

### ***Description***

This step plots the time-domain waveforms of the combined signals for both normal hearing and simulated hearing loss.

### ***Functions Used:***

1. **plot**: Creates a 2D line plot of the time-domain signals.
  - `plot((0:length(combinedSignal)-1)/fs, combinedSignal);`
2. **xlabel, ylabel, title**: Labels the x-axis y-axis, and sets the plot title.
  - `xlabel('Time (s)'); ylabel('Amplitude'); title('Time-Domain Waveform of Combined Signal (Normal Hearing)');`
3. **subplot**: Creates axes in tiled positions for multiple plots in a single figure.
  - `subplot(2, 1, 1);`

## ***Step 3: Composite Frequency Spectrum***

### ***Description***

This step computes the combined signals' Fast Fourier Transform (FFT) and plots the frequency spectra for normal and simulated hearing loss.

### ***Functions Used:***

1. **fft**: Computes the Fast Fourier Transform of the signals.
  - `fftCombinedSignal = fft(combinedSignal);`
2. **abs**: Computes the magnitude of the FFT.
  - `amplitude = abs(fftCombinedSignal)/N;`

3. **plot:** Creates a 2D line plot of the frequency spectra.
  - `plot(f, amplitude);`
4. **xlabel, ylabel, title:** Labels the x-axis y-axis, and sets the plot title.
  - `xlabel('Frequency (Hz)');, ylabel('Amplitude');, title('Composite Frequency Spectrum of Combined Signal (Normal Hearing)');`
5. **xlim:** Sets the x-axis limits for the current axes.
  - `xlim([0, max(frequencies)*1.2]);`
6. **subplot:** Creates axes in tiled positions for multiple plots in a single figure.
  - `subplot(2, 1, 1);`

## ***Step 4: Play Tones Again at New Amplitudes to Simulate Hearing Loss***

### ***Description***

This step plays the combined signal with simulated hearing loss to provide an auditory comparison of how the tones would sound after applying the hearing loss filter.

### ***Functions Used:***

1. **sound:** Plays the combined signal with hearing loss.
  - `sound(combinedSignalHearingLoss, fs);`
2. **pause:** Pauses execution to allow the sound to finish playing.
  - `pause(length(combinedSignalHearingLoss)/fs + 1);`

Then you will want to save the script and then click Run. Ensure you have your speakers on your device and the volume is up. You hear the sounds two times before the script is finished running. You should notice that as the frequencies get higher, they get lower. The type of hearing loss simulated in this script is sensorineural hearing loss. Sensorineural hearing loss occurs due to damage to the inner ear's cochlear or auditory nerve pathway. It is the most common type of permanent hearing loss. The causes of this type of hearing loss can range and include gaining, exposure to loud noise, genetic factors, and diseases or infections. The main symptom of this hearing loss is loss of higher frequencies. With the loss pass filter used in the script, we can attenuate the higher frequencies, mimicking the characteristics of sensorineural hearing loss. You will notice that the script also generates two figures. Let's start with Figure 1, the Time Domain Signals. Fig. 11.6 is what it looks like.

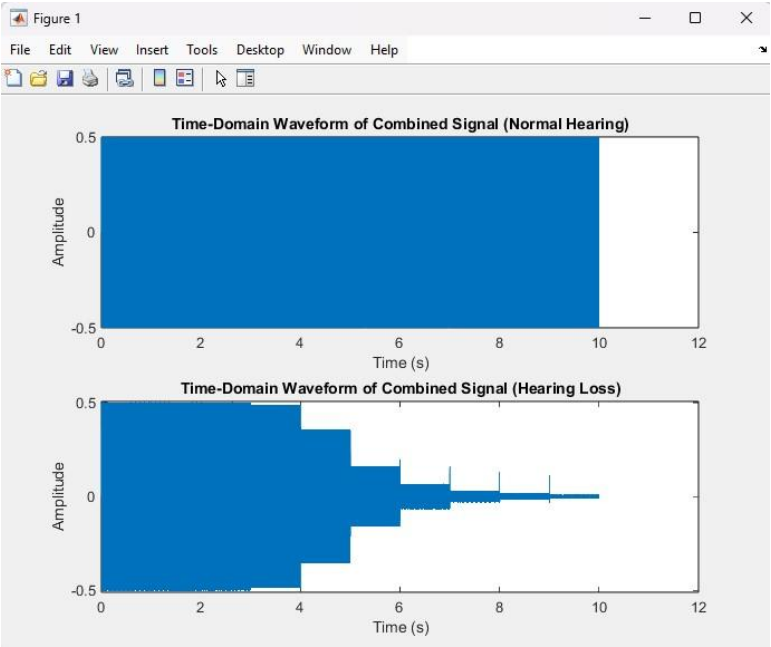


Figure 11.6: Time Domain Wave forms for Normal Hearing vs Hearing Loss

The figure displays the time-domain waveforms of two combined audio

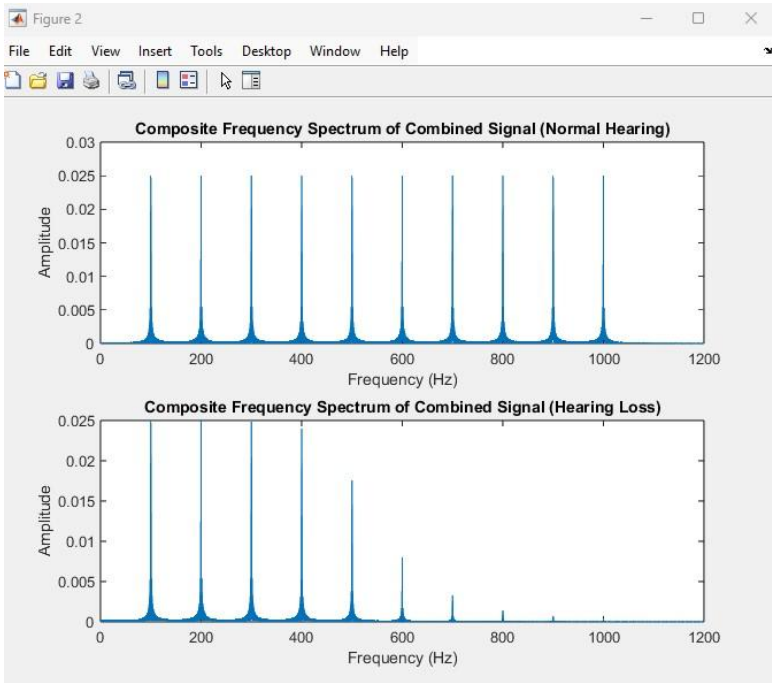


Figure 11.7: Composite Frequency for Normal Hearing vs Hearing Loss

signals: one representing normal hearing and the other simulating sensorineural hearing loss. The top plot shows the waveform for normal hearing, where the amplitude remains consistent across the entire duration of approximately 10 seconds. This indicates that the generated sine wave tones, which are concatenated, maintain their integrity without any attenuation. In contrast, the bottom plot illustrates the waveform for the signal with simulated hearing loss. Here, the amplitude diminishes significantly over time, particularly after the initial few seconds. The result is a noticeable decrease in the signal's amplitude, especially for the higher frequencies, which manifests as a progressively weaker waveform. This visual representation effectively highlights the impact of sensorineural hearing loss on audio signals,

demonstrating how higher frequencies are diminished, leading to a loss of clarity and intensity in the sound.

Now let's look at Fig. 11.7, the Composite Frequency Spectrum. Here is what it looks like. The figure illustrates the composite frequency spectra of two combined audio signals: one for normal hearing and the other simulating sensorineural hearing loss. In the top plot, representing normal hearing, there are distinct and relatively uniform peaks at the frequencies where the original sine wave tones were generated—specifically at 100 Hz, 200 Hz, 300 Hz, 400 Hz, 500 Hz, 600 Hz, 700 Hz, 800 Hz, 900 Hz, and 1000 Hz. This indicates that each tone is preserved with its original intensity, reflecting an ideal, undistorted signal where all frequency components are present as expected.

In contrast, the bottom plot, representing the signal with simulated hearing loss, shows that the peaks at lower frequencies (100 Hz, 200 Hz, 300 Hz, 400 Hz, and 500 Hz) remain prominent. However, the peaks at higher frequencies (above 500 Hz) are significantly attenuated or almost nonexistent. This attenuation is due to applying a low-pass filter, which mimics the effect of sensorineural hearing loss by reducing the sensitivity to higher frequencies. The comparison between the two plots demonstrates the impact of sensorineural hearing loss on the frequency content of the audio signal, effectively visualizing the loss of higher-frequency components. This is the conclusion to this lab example. We encourage you to visit our [GitHub page](#) for more practical lab examples.





## Chapter 12

# The Battle Frontier: Fighting Neurological Disorders

# Chapter Introduction and Learning Objectives

Neurological disorders encompass various conditions that affect the nervous system, including the brain, spinal cord, and peripheral nerves. These disorders can significantly impact the lives of individuals, families, and society, leading to profound challenges in daily functioning and overall well-being. By the end of this chapter, you will be able to:

1. *Recognize and describe the key characteristics and symptoms of major neurological disorders, including Alzheimer's disease, Parkinson's disease, Autism Spectrum Disorder (ASD), Multiple Sclerosis (MS), Dementia, Huntington's disease, and Amyotrophic Lateral Sclerosis (ALS).*
2. *Understand the physiological explanations underlying each neurological disorder, including the roles of genetic and environmental factors in their development and progression.*
3. *Gain insights into how advanced technologies, such as imaging techniques, wearable devices, AI, and telemedicine, are used to diagnose, treat, and manage these disorders.*
4. *Understand the social and economic implications of neurological disorders, including the burden on healthcare systems, and recognize the importance of early intervention and support in alleviating this burden and improving the lives of those affected.*
5. *Learn about emerging trends and future research directions, including neuroprotective therapies, personalized medicine, and the potential of new technologies to transform neurological care.*

The burden of neurological disorders is immense, not only due to the direct healthcare costs but also the indirect costs, such as lost productivity and reduced quality of life. As our understanding of these disorders has evolved, so has the technology available to diagnose, treat, and manage them. Recent advancements offer hope for better patient outcomes and an improved quality of life for those affected. As we delve into the profiles of these major neurological disorders, we will explore their distinct characteristics,

underlying mechanisms, and innovative technological interventions that are changing the landscape of treatment and management. Let us begin with an in-depth look at these conditions, starting with Alzheimer's disease.

## **Detailed Disorder Profiles**

### ***Alzheimer's Disease: A Complex Neurodegenerative Disorder***

Alzheimer's disease (AD) is a progressive and irreversible neurological disorder that affects memory, thinking, and behavior. It is the most common form of dementia, accounting for 60-80% of dementia cases. AD is characterized by a decline in cognitive function, including memory loss, language difficulties, and problem-solving impairments [240]. As the disease progresses, individuals with AD may experience changes in personality, mood, and behavior, leading to a loss of functional abilities and independence [241].

### ***Pathophysiological Mechanisms***

The exact causes of AD are still not fully understood, but research has identified several key pathophysiological mechanisms. One of the hallmark features of AD is the accumulation of amyloid-beta plaques outside neurons, which disrupts communication between brain cells and leads to cell death. Additionally, the formation of tau tangles inside neurons disrupts the transport system and contributes to neuronal damage. Brain atrophy, particularly in the hippocampus and temporal lobe, is also a characteristic feature of AD [240]. Furthermore, inflammation and oxidative stress have been implicated in the pathogenesis of AD, with activation of immune cells and release of inflammatory chemicals contributing to neuronal damage [242].

### ***Risk Factors and Contributing Factors***

While the exact causes of AD are still unknown, several risk factors and contributing factors have been identified. Genetic factors, such as the APOE  $\epsilon 4$  allele and mutations in APP, PSEN1, and PSEN2 genes, increase the risk of developing AD [241]. Environmental and lifestyle factors, including age, cardiovascular health, head injuries, physical inactivity, smoking, and poor

diet, also contribute to the risk of AD. Social engagement and cognitive reserve have also been shown to play a role in AD risk, with low social engagement and loneliness increasing risk and higher cognitive reserve delaying onset [243].

### ***Current Understanding and Future Directions***

Despite significant advances in our understanding of AD, much remains to be discovered. Current research is focused on developing effective treatments and prevention strategies, including immunotherapies targeting amyloid-beta and tau and lifestyle interventions aimed at reducing risk factors. A comprehensive understanding of the complex interplay between genetic, environmental, and lifestyle factors will be crucial in developing effective prevention and treatment strategies for AD.

#### ***Infographic Summary:***

- Symptoms: Memory loss, confusion, difficulty with language, disorientation, mood swings, and behavioral changes.
- Stages: Mild (early-stage), moderate (middle-stage), and severe (late-stage).
- Statistics: It affects approximately 50 million people worldwide; the incidence is expected to triple by 2050.
- Key Biomarkers: Amyloid-beta plaques, tau tangles, and brain atrophy.

## **Parkinson's Disease**

### ***A Progressive Movement Disorder***

Parkinson's disease (PD) is a chronic and progressive neurodegenerative disorder that primarily affects motor function. It is the second most common neurodegenerative disease after Alzheimer's, characterized by symptoms such as tremors, rigidity, bradykinesia (slowness of movement), and postural instability [244]. Non-motor symptoms, including cognitive impairment, mood disorders, sleep disturbances, and autonomic dysfunction, are also prevalent [245]. The progression of PD varies, but it generally leads to a significant decline in quality of life and functional independence.

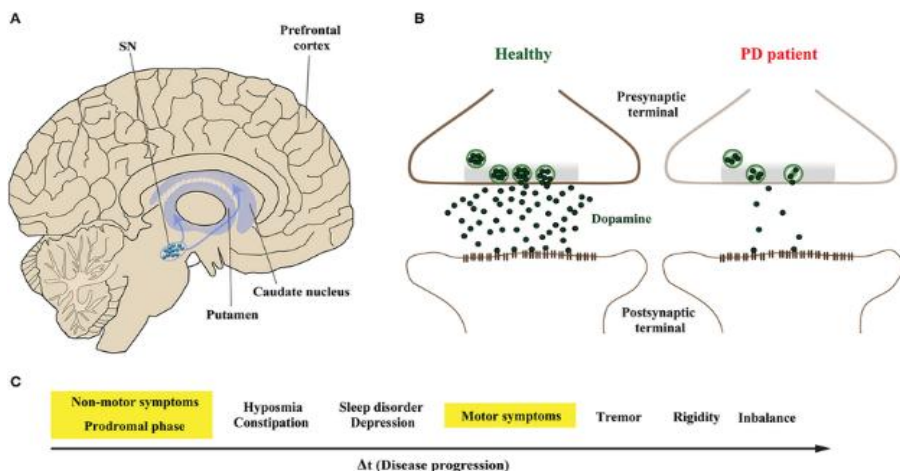


Figure 12.1: (A) loss of dopaminergic (DA) neurons in the substantia nigra (SN), (B) Healthy vs PD Patient presynaptic terminal, (C) resulting motor symptoms [246]

## Pathophysiological Mechanisms

The hallmark of PD is the degeneration of dopaminergic neurons, shown in Fig. 12.1 [246], in the substantia nigra, a region of the brain that plays a crucial role in regulating movement. The loss of these neurons leads to a significant decrease in dopamine levels, disrupting normal communication between the brain and muscles and resulting in the motor symptoms characteristic of PD [247]. Another key feature of PD is the presence of Lewy bodies—abnormal aggregates of alpha-synuclein protein within neurons. These aggregates are toxic to cells and contribute to neurodegeneration [248]. Recent research also suggests a potential gut-brain axis involvement, where misfolded alpha-synuclein may originate in the gastrointestinal tract and travel to the brain via the vagus nerve, implicating the gut in PD pathogenesis [249].

## Risk Factors and Contributing Factors

PD's etiology (cause) involves genetic and environmental factors. Genetic mutations in genes such as LRRK2, PARK2, and SNCA increase the risk of developing PD, although these account for only a small percentage of cases

[244]. Environmental factors, including exposure to pesticides, heavy metals, and solvents, have been associated with a higher risk of PD [250]. Additionally, age is the most significant risk factor, with most cases occurring in individuals over 60. There is also evidence that rural living and farming occupations, likely due to increased exposure to agricultural chemicals, are associated with higher PD prevalence [250].

### ***Current Understanding and Future Directions***

While there is currently no cure for PD, various treatments aim to manage symptoms and improve quality of life. Medications such as levodopa (L-Dopa) and dopamine agonists are commonly used to replace or mimic dopamine, alleviating motor symptoms [244]. Deep brain stimulation (DBS) is a surgical intervention that can relieve some patients. Despite hope in these symptomatic-based treatments, some significant side effects accompany them. Some are loss of efficacy over time, hallucinations, involuntary and compulsive behaviors, and involuntary movements. Future research is focused on understanding the mechanisms of alpha-synuclein aggregation, exploring neuroprotective strategies, and investigating the potential role of the gut microbiome in PD. Rather than just addressing symptoms, developing treatments that modify the disease course remains a critical goal.

#### ***Infographic Summary:***

- Symptoms: Tremors, muscle rigidity, bradykinesia, postural instability, cognitive impairment, mood disorders, and sleep disturbances.
- Stages: Early-stage, mid-stage, and advanced-stage.
- Statistics: It affects over 10 million people worldwide and is more common in men than women.
- Key Biomarkers: Dopaminergic neuron loss, Lewy bodies, and reduced dopamine levels.

# **Autism Spectrum Disorder (ASD)**

## ***A Complex Developmental Condition***

Autism Spectrum Disorder (ASD) is a developmental disorder that affects communication, behavior, and social interaction. The term "spectrum" reflects the wide range of symptoms and severity observed among individuals with ASD [251]. Core features include difficulties in social communication, restricted interests, and repetitive behaviors. ASD can present with various cognitive abilities, from intellectual disability to high functioning. Still, there is a range of symptoms associated with ASD that may be different from male to female [251].

## ***Pathophysiological Mechanisms***

ASD is associated with atypical brain development, including differences in structure and connectivity. These neurodevelopmental anomalies may affect neural circuits involved in social communication and behavior [252]. Genetic factors play a significant role in ASD, with many implicated genes affecting synaptic function and neural development [253]. Environmental factors, such as prenatal exposures to certain drugs, infections, or toxins, may also contribute to the risk [254]. Epigenetic mechanisms, which involve changes in gene expression without altering the DNA sequence, are thought to play a role in how genetic and environmental factors influence brain development in ASD [255].

## ***Risk Factors and Contributing Factors***

ASD has a strong genetic component, with heritability estimates ranging from 50% to 90% [253]. Several genetic syndromes, such as Fragile X syndrome and Rett syndrome, are associated with a higher risk of ASD [251]. Environmental factors during pregnancy, including maternal infections and exposure to certain chemicals, have been linked to ASD. Advanced parental age, particularly in fathers, has also increased risk [254]. The disorder is more commonly diagnosed in males, with a male-to-female ratio of approximately 4:1 [251].

## ***Current Understanding and Future Directions***

ASD diagnosis typically involves behavioral assessments and developmental history. Early intervention, including behavioral therapies and educational support, can significantly improve outcomes. Current research focuses on understanding the underlying genetic and neurobiological mechanisms of ASD, developing biomarkers for earlier and more accurate diagnosis, and exploring new therapeutic interventions. Advances in technology, such as AI for behavioral analysis and VR for social skills training, promise to enhance the lives of individuals with ASD.

### ***Infographic Summary:***

- Symptoms: Challenges in social interaction, communication difficulties, repetitive behaviors, and restricted interests.
- Diagnostic Criteria: Based on behavioral observations and developmental history.
- Statistics: It affects 1 in 54 children in the United States; it is more common in boys than girls.
- Key Biomarkers: Abnormal brain connectivity, structural differences in the brain, and genetic mutations.

## **Multiple Sclerosis (MS)**

### ***An Autoimmune and Neurodegenerative Disorder***

Multiple Sclerosis (MS) is a chronic autoimmune disorder that affects the central nervous system (CNS), leading to demyelination and neurodegeneration. It has various symptoms, including motor and sensory impairments, visual disturbances, and cognitive changes. The course of the disease can vary, with some individuals experiencing relapsing-remitting episodes and others progressing to a more severe form known as secondary progressive MS [256].

### ***Pathophysiological Mechanisms***

MS involves an immune-mediated attack on the myelin sheath (Chapter 1), the protective covering around nerve fibers in the CNS. This demyelination

disrupts the transmission of electrical impulses along the nerves, leading to symptoms such as muscle weakness, spasticity, and sensory disturbances [257]. In addition to demyelination, MS can cause axonal damage and neuronal loss, contributing to permanent neurological deficits [258]. The disease is associated with chronic inflammation, involving T and B cells that cross the blood-brain barrier and attack CNS components [257]. Neurodegeneration, resulting from chronic inflammation and immune-mediated damage, is a significant aspect of MS pathology [258].

### ***Risk Factors and Contributing Factors***

Genetic factors play a role in MS, with specific genetic variations, particularly in the HLA-DRB1\*15:01 allele, associated with increased susceptibility [259]. Environmental factors also contribute to MS risk, including viral infections (such as Epstein-Barr virus), vitamin D deficiency, and smoking. Geographic factors are notable, with higher MS prevalence observed in regions farther from the equator, suggesting a link to sunlight exposure and vitamin D levels [260].

### ***Current Understanding and Future Directions***

MS is typically diagnosed through clinical evaluation, MRI, and cerebrospinal fluid analysis. Disease-modifying therapies (DMTs) are available to reduce the frequency and severity of relapses and slow disease progression. Current research focuses on understanding the mechanisms of immune dysregulation and neurodegeneration in MS, developing more effective DMTs, and exploring strategies for promoting remyelination and neuroprotection. Advances in imaging and biomarker discovery are also key focus areas, aiming to improve early diagnosis and treatment monitoring.

### ***Infographic Summary:***

- Symptoms: Fatigue, motor and sensory impairments, vision problems, cognitive dysfunction, and balance issues.
- Types: Relapsing-remitting MS (RRMS), secondary progressive MS (SPMS), primary progressive MS (PPMS).

- Statistics: It affects approximately 2.8 million people worldwide, more common in women than men.
- Key Biomarkers: Demyelination, oligoclonal bands in cerebrospinal fluid (CSF), and MRI-detected lesions.

## **Amyotrophic Lateral Sclerosis (ALS)**

### ***A Degenerative Motor Neuron Disease***

Amyotrophic Lateral Sclerosis (ALS), also known as Lou Gehrig's disease, is a progressive neurodegenerative disorder that primarily affects motor neurons. These neurons control voluntary muscles, and degeneration leads to muscle weakness, atrophy, and, eventually, paralysis. The disease progresses rapidly, with most patients succumbing to respiratory failure within 3-5 years of diagnosis [261].

### ***Pathophysiological Mechanisms***

ALS involves the degeneration of both upper motor neurons (in the brain) and lower motor neurons (in the brainstem and spinal cord). This degeneration disrupts the transmission of signals from the brain to the muscles, resulting in the progressive loss of motor function [262]. The presence of abnormal protein aggregates, such as TDP-43, SOD1, and FUS, is a common pathological feature in ALS, contributing to neuronal toxicity and cell death [263]. Elevated levels of glutamate, an excitatory neurotransmitter, have been implicated in ALS, causing excitotoxicity and further neuronal damage. Oxidative stress and mitochondrial dysfunction are also involved, contributing to the pathogenesis and progression of the disease. The stages of ALS can be seen in Table 12.1 [264].

### ***Risk Factors and Contributing Factors***

Approximately 10% of ALS cases are familial, meaning they are inherited. Several genetic mutations have been identified, including those in the SOD1, C9orf72, TARDBP, and FUS genes, with C9orf72 being the most common genetic cause [265]. Environmental factors may also contribute to ALS risk, including exposure to toxins, heavy metals, pesticides, and physical trauma.

Smoking and a history of intense physical activity have been associated with increased risk. The disease is more commonly diagnosed in individuals between 40 and 70 and is slightly more prevalent in men [261].

Table 12.1: Stages of ALS and its associated Symptoms and Physical Effects [259]

Stage	Symptoms	Physical Effects
Early	Muscle weakness, fasciculations, and atrophy are often limited to one body region.	Fatigue, poor balance, slurred words, tripping, and weak grip
Middle	The symptoms seen in the early stages are more widespread and affect more than one body region. Muscles become paralyzed, and fasciculations continue.	Muscle contractures, weakness in breathing and swallowing causing difficulty eating, drinking, and breathing
Late	Most voluntary muscles are paralyzed, and the breathing muscles are very weak.	Very limited mobility, poor respiration causing fatigue, and increased susceptibility to pneumonia. Loss of speech and limited eating/drinking via mouth

***Current Understanding and Future Directions***

There is currently no cure for ALS, and treatment focuses on managing symptoms and improving quality of life. Riluzole and edaravone are the only FDA-approved drugs that modestly extend survival or slow disease progression. Non-invasive ventilation (NIV) and other supportive therapies can help manage respiratory complications and maintain communication

abilities. Current research focuses on understanding the genetic and molecular mechanisms underlying ALS, developing neuroprotective and neurorestorative therapies, and exploring potential treatments such as gene and stem cell therapy.

## **Dementia**

### ***A Spectrum of Neurodegenerative Disorders***

Dementia is an umbrella term used to describe a range of neurodegenerative conditions characterized by progressive cognitive decline and impairment in daily functioning. The most common type of dementia is Alzheimer's disease, followed by vascular dementia, Lewy body dementia, and frontotemporal dementia [241]. Dementia affects memory, thinking, behavior, and the ability to perform everyday activities.

### ***Pathophysiological Mechanisms***

#### ***Alzheimer's Disease Pathology***

Alzheimer's disease is characterized by the accumulation of amyloid-beta plaques and tau protein tangles in the brain, which disrupt neuronal communication and lead to cell death and brain atrophy [265].

#### ***Vascular Dementia***

This type of dementia results from reduced blood flow to the brain, often due to strokes or other vascular issues, leading to ischemic damage and cell death [266].

#### ***Lewy Body Dementia***

In this condition, abnormal clumps of alpha-synuclein protein, known as Lewy bodies, are present in the brain. These contribute to cognitive decline, motor symptoms like Parkinson's disease, and vivid hallucinations[267].

#### ***Frontotemporal Dementia***

This form of dementia involves degeneration of the frontal and temporal lobes, affecting personality, behavior, and language abilities [268].

## ***Risk Factors and Contributing Factors***

Genetic factors contribute to the risk of developing dementia, with mutations in specific genes associated with early-onset forms of Alzheimer's disease and other dementias. Cardiovascular risk factors, such as hypertension, diabetes, and high cholesterol, are significant contributors, particularly for vascular dementia [266]. Lifestyle factors, including diet, physical activity, and cognitive engagement, also play crucial roles in the risk of developing dementia [241]. Age is the most significant risk factor, with the prevalence of dementia increasing significantly in individuals over the age of 65.

## ***Current Understanding and Future Directions***

Diagnosis of dementia involves a combination of medical history, cognitive testing, and imaging techniques. There is currently no cure for dementia, and treatments focus on managing symptoms and slowing disease progression. Research is ongoing to understand the underlying mechanisms of various types of dementia, develop biomarkers for early diagnosis, and explore potential disease-modifying therapies. Advances in personalized medicine and technology, such as cognitive training programs and AI-powered diagnostic tools, offer hope for better management and improved outcomes for individuals with dementia.

### ***Infographic Summary:***

- Symptoms: Memory loss, confusion, language difficulties, impaired judgment, and changes in behavior and personality.
- Types: Alzheimer's disease, vascular dementia, Lewy body dementia, frontotemporal dementia.
- Statistics: It affects approximately 50 million people worldwide and is expected to increase as the population ages.
- Key Biomarkers: Varies by type; includes amyloid-beta plaques, tau tangles, Lewy bodies, and ischemic lesions.

# Huntington's Disease

## *A Hereditary Neurodegenerative Disorder*

Huntington's disease (HD) is a progressive neurodegenerative disorder caused by a genetic mutation. It is characterized by motor, cognitive, and psychiatric symptoms. The disease typically manifests in mid-adulthood and progressively worsens over time, leading to significant disability and early death [269]. The prevalence of HD is estimated to be about 5-10 cases per 100,000 individuals of European descent [270].

## *Pathophysiological Mechanisms*

HD is caused by an expanded CAG repeat in the HTT gene, which encodes the huntingtin protein. Individuals with more than 36-40 CAG repeats in the HTT gene will invariably develop the disease [38]. This expansion produces an abnormally long polyglutamine tract in the huntingtin protein, causing it to misfold and form toxic aggregates in neurons [271]. These aggregates disrupt normal cellular processes, including transcriptional regulation, mitochondrial function, and protein degradation pathways, leading to neuronal dysfunction and death [271]. The most affected brain regions are the striatum and cerebral cortex, which are crucial for motor control and cognitive functions [272].

## *Risk Factors and Contributing Factors*

HD is inherited in an autosomal dominant manner, meaning an individual only needs one copy of the mutated gene from one parent to develop the disease. The number of CAG repeats in the HTT gene correlates with the age of onset and severity of symptoms; a higher number of repeats is associated with an earlier onset and more severe disease course [273]. Unlike many other neurodegenerative disorders, environmental factors do not significantly influence the onset or progression of HD, as the disease's course is primarily determined by genetic factors [274].

## *Current Understanding and Future Directions*

There is currently no cure for HD, and treatment primarily focuses on managing symptoms. Medications such as tetrabenazine can help control

chorea (involuntary movements), while antipsychotics and antidepressants are used to manage psychiatric symptoms. Ongoing research is exploring potential disease-modifying therapies, including gene silencing techniques, such as antisense oligonucleotides and RNA interference, to reduce the production of the mutant huntingtin protein. Additionally, studies are investigating neuroprotective strategies and the use of stem cell therapies to replace lost neurons and restore brain function.

### ***Infographic Summary:***

- Symptoms: Involuntary movements (chorea), impaired coordination, cognitive decline, mood swings, and psychiatric symptoms.
- Stages: Early-stage, mid-stage, and late-stage.
- Statistics: It affects approximately 5-10 per 100,000 people worldwide.
- Key Biomarkers: Genetic testing for HTT gene mutation, MRI showing brain atrophy.

## **Impact on Society**

Neurological disorders have a profound impact on individuals, families, and society. The effects of these disorders extend far beyond the patients themselves, affecting employers, caregivers, physicians, insurance companies, and regulatory bodies. For instance, patients with neurological disorders often experience a reduced quality of life due to cognitive decline, mobility issues, and emotional distress. This can lead to a loss of independence and autonomy, increasing the risk of comorbidities and secondary health conditions [275]. Furthermore, the emotional and psychological burden of neurological disorders should not be underestimated, with anxiety, depression, and stigma being common comorbidities.

Caregivers, often family members or friends, also bear a significant burden. The emotional strain and stress of caring for a loved one can be overwhelming, leading to physical demands such as sleep disturbances and fatigue.

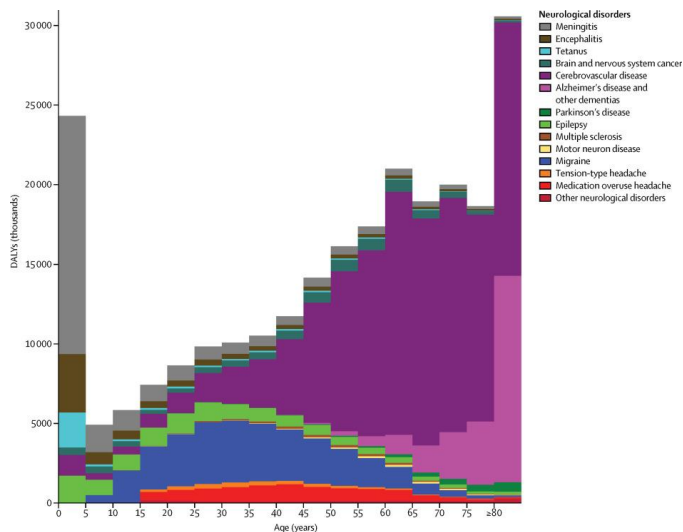


Figure 12.2: DALYs by age group and categorized by disorders [278]

Additionally, caregivers may experience a financial burden due to reduced income, increased expenses, and lost productivity. Social isolation and reduced social connections are also common consequences of caregiving, highlighting this critical group's need for support and resources [276].

Employers are also impacted by neurological disorders, with reduced productivity and absenteeism being common consequences of employees caring for loved ones. Increased healthcare costs and insurance premiums are additional burdens, with a potential loss of skilled and experienced employees due to caregiving responsibilities [277]. As such, employers must consider accommodations and support for employees with neurological disorders, ensuring a healthy and productive work environment.

Physicians, too, face unique challenges in caring for patients with neurological disorders. The emotional toll of caring for patients with debilitating and incurable conditions should not be underestimated, with complexities of diagnosis, treatment, and management adding to the burden [40]. Staying current with the latest research, treatments, and guidelines is essential while balancing patient care with administrative and regulatory responsibilities. This

is especially critical in rural communities, low-income areas, and low-income countries where access to specialized care is not readily available.

Insurance companies face increased costs due to healthcare services, long-term care, and prescription medications, and they face challenges in assessing and managing risk for neurological disorders. Specialized programs and services for patients with neurological disorders are essential, and if not managed effectively, they can potentially increase premiums and reduce coverage [276].

Regulatory bodies are critical in developing and implementing policies and guidelines for neurological disorders, ensuring patient and caregiver access to care, services, and support [275]. Monitoring and addressing healthcare disparities and inequities is essential, balancing individual needs with societal and economic considerations a delicate task.

The economic impact of neurological disorders is substantial, with estimated annual costs of \$305 billion for Alzheimer's disease [241], \$52 billion for Parkinson's disease (Parkinson's Foundation, 2022, \$15 billion for epilepsy [277], and \$10 billion for multiple sclerosis [276]. These figures highlight the need for continued research, support, and resources to address the complex needs of patients, caregivers, and society. The DALYs (Disability-adjusted life years) refer to years of healthy life lost due to premature death and disability (Fig. 12.2 [278]) and are a good comparison to the burden of disease.

## **Technological Interventions in Neurological Disorders**

### ***The Role of Technology***

Technological advancements have significantly impacted the field of neuroengineering, providing innovative tools for diagnosing, treating, and managing neurological disorders. These advancements span various technologies, including advanced imaging techniques, wearable devices, artificial intelligence (AI), and machine learning (ML). Integrating these technologies into clinical practice can revolutionize neurological care, offering more precise diagnostics, personalized treatments, and improved patient outcomes.

## ***Advanced Imaging Techniques***

Advanced imaging techniques, such as magnetic resonance imaging (MRI) (Chapter 5), positron emission tomography (PET), and functional MRI (fMRI) (Chapter 5), have enhanced the ability to diagnose and monitor neurological disorders. These modalities provide detailed insights into brain structure and function, facilitating early detection of abnormalities and precise tracking of disease progression. For instance, MRI and PET scans are commonly used in diagnosing and monitoring Alzheimer's disease, allowing visualization of amyloid plaques and tau tangles—key biomarkers of the disease [241]. These imaging technologies are also vital in assessing structural and functional changes in Parkinson's disease, multiple sclerosis, and other neurodegenerative conditions [240].

## ***Wearable Devices***

Wearable devices have gained prominence in managing neurological disorders, continuously monitoring physiological parameters such as heart rate, movement, and sleep patterns. These devices provide valuable data for patients and clinicians, enabling more accurate disease management. In Parkinson's disease, wearable sensors can track motor symptoms like tremors and bradykinesia, aiding treatment optimization [279]. Similarly, wearable devices monitor and manage epilepsy by detecting and recording seizure activity, allowing timely interventions.

## ***Artificial Intelligence and Machine Learning***

AI and ML technologies, Discussed in Chapter 3, are increasingly employed in diagnosing and treating neurological disorders. These technologies can analyze large datasets to identify patterns and predict outcomes, potentially leading to earlier diagnoses and more personalized treatment plans. For example, AI algorithms have been developed to predict the onset of Alzheimer's disease using imaging and genetic data [83]. Additionally, ML models optimize deep brain stimulation (DBS) parameters in Parkinson's disease, enhancing the efficacy of this treatment [280]. The application of AI extends to various disorders, including multiple sclerosis and dementia, where

it aids in diagnosing, monitoring disease progression, and developing individualized treatment strategies.

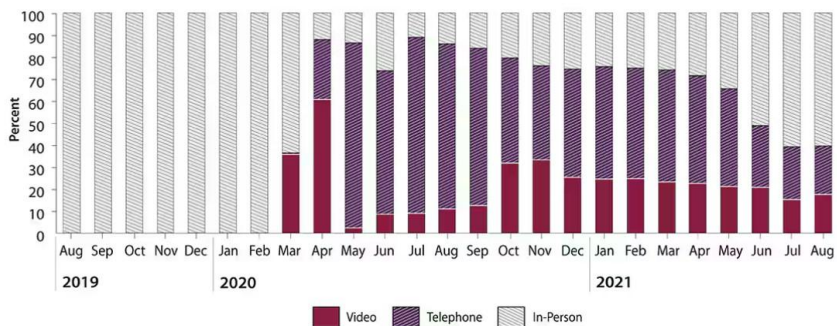


Figure 12.3: Telemedicine Growth During Covid-19 between 2019 and 2021 [281]

## Telemedicine

The adoption of telemedicine has been accelerated by the COVID-19 pandemic [281], which has proven to be a valuable tool for managing neurological disorders (Fig. 12.3 [281]). Telemedicine platforms enable remote consultations with neurologists, reducing the need for travel and improving access to care, particularly for patients with mobility issues or those in remote areas. Studies have demonstrated the effectiveness of telemedicine in managing conditions such as epilepsy, multiple sclerosis, and headache disorders, providing continuous care and monitoring [282].

## Technological Interventions by Disorder

### Alzheimer's Disease

#### Current Technology

1. Brain Imaging Techniques: MRI and PET scans are integral in detecting brain changes associated with Alzheimer's disease. These technologies help identify brain atrophy and the presence of amyloid-beta plaques and tau tangles [241].

2. **Wearable Devices:** Devices that monitor cognitive function and daily activities can detect early signs of cognitive decline, providing continuous patient monitoring [283].
3. **AI-Based Diagnostic Tools:** AI and ML algorithms analyze medical imaging and genetic data to improve diagnostic accuracy, facilitating early and precise diagnoses [284].

### Future Directions

Research is focused on developing neuroprotective drugs to slow or halt disease progression. Advances in biomarker identification could enable earlier diagnoses, while personalized medicine approaches tailored to individual genetic profiles are being explored to enhance treatment effectiveness.

## ***Parkinson's Disease***

### Current Technology

1. **Deep Brain Stimulation (DBS):** DBS involves implanting electrodes in specific brain areas to regulate abnormal brain activity, significantly improving motor symptoms in Parkinson's patients [280].
2. **Wearable Sensors:** These devices monitor motor symptoms and provide real-time data, assisting clinicians in adjusting treatment plans and medications more accurately [285].
3. **Mobile Apps:** Apps help manage medication schedules, track symptoms, and provide exercise routines, supporting patients in maintaining structured care routines.

### Future Directions

Future research in Parkinson's focuses on gene therapy and stem cell therapy. Gene therapy aims to correct genetic mutations, while stem cell therapy seeks to replace lost dopaminergic neurons. Neurorestorative therapies are also being explored to repair damaged neural circuits.

## ***Autism Spectrum Disorder (ASD)***

### **Current Technology**

1. Assistive Communication Devices: Augmentative and alternative communication (AAC) devices, including speech-generating devices and apps, facilitate communication for individuals with ASD [286].
2. Virtual Reality (VR): VR technology creates immersive environments for practicing social interactions and developing social skills [226].
3. AI-Based Behavioral Analysis: AI algorithms analyze behavioral data, identifying patterns and providing insights for more effective behavior intervention plans [287].

### **Future Directions**

Ongoing research aims to develop advanced genetic testing for early detection and personalized intervention programs tailored to each individual's genetic profile. AI continues to enhance the accuracy and effectiveness of behavioral interventions.

## ***Multiple Sclerosis (MS)***

### **Current Technology**

1. MRI for Disease Monitoring: MRI is the gold standard for diagnosing and monitoring MS, providing detailed images of brain and spinal cord lesions [288].
2. Disease-Modifying Therapies (DMTs): DMTs reduce relapse frequency and disease progression, targeting the immune system to prevent myelin damage [289].
3. Telemedicine: Telemedicine facilitates remote consultations, improves access to care, and enables regular monitoring [290].

### **Future Directions**

Future research aims to develop advanced immunotherapies and neuroprotective agents to prevent or repair myelin damage. Remyelination strategies are also being explored to restore function.

## ***Dementia***

### **Current Technology**

1. **Cognitive Training Programs:** Computer-based programs improve memory, attention, and executive function in individuals with dementia [291].
2. **GPS Tracking Devices:** These devices monitor the location of individuals who may wander, enhancing safety [292].
3. **AI and Robotics:** AI-powered virtual assistants and robotic companions offer cognitive and social support, improving quality of life [293].

### **Future Directions**

Research is focused on developing more advanced cognitive training programs leveraging VR and gamification. AI is being explored to predict disease progression and tailor interventions.

## ***Huntington's Disease***

### **Current Technology**

1. **Genetic Testing:** Genetic testing is crucial for diagnosing Huntington's disease and assessing risk in individuals with a family history [269].
2. **Symptomatic Treatments:** Medications such as tetrabenazine manage motor symptoms, while antipsychotics address psychiatric issues [294].
3. **Telemedicine:** Telemedicine platforms provide access to specialized care, support regular monitoring, and reduce the need for travel.

### **Future Directions**

Research focuses on developing disease-modifying therapies targeting the genetic mutation responsible for Huntington's. Gene editing technologies, such as CRISPR, hold promise for correcting the mutation and potentially halting disease progression.

## Future Directions

In the coming years, advancements in neuroengineering are expected to significantly improve our understanding, diagnosis, and treatment of neurological disorders. One exciting area of development is neuroprotective and neurorestorative therapies. These treatments aim to protect neurons from damage and potentially restore lost functions in conditions like Alzheimer's and Parkinson's disease. Imagine being able to slow down or even stop the progression of these diseases, giving people more time with their loved ones and a better quality of life.

Another promising direction is the use of biomarkers for early diagnosis and monitoring. Biomarkers are measurable indicators found in blood, cerebrospinal fluid, or even through imaging. They can provide valuable information about what's happening in the brain, sometimes before symptoms start. Early detection can lead to earlier treatments, which might slow down or alter the course of the disease, offering a critical intervention window.

The integration of genomics and personalized medicine into treatment plans is another game-changer. By understanding a patient's genetic makeup, doctors can tailor treatments to suit their needs, potentially leading to better outcomes. This is especially relevant for diseases with a genetic component, like Huntington's disease. Personalized medicine is about more than just using the right drugs—it's about finding the right treatments at the right time for everyone.

Brain-computer interfaces (BCIs) and neural prosthetics also push the boundaries of what's possible. BCIs create a direct communication pathway between the brain and external devices, which can help people with conditions like ALS regain some control over their environment. Neural prosthetics, like cochlear implants, are already assisting people to restore lost senses, and new developments promise even more exciting applications.

## Chapter 12: Summary

Neurological disorders are challenging for everyone involved, from the patients and their families to the healthcare professionals providing care. The increasing prevalence of these conditions and the growing older population

make it clear that we must continue to push forward with research and development in this field to relieve the burden on healthcare systems and society.

For those of you in neuroengineering, this is an incredibly exciting time. There's so much potential to make a real difference in people's lives. Whether you're interested in developing new diagnostic tools, working on cutting-edge therapies, or improving existing technologies, there's a place for your skills and creativity.

Researchers and healthcare professionals need to stay updated on the latest advancements and be ready to incorporate new tools and treatments into their practice. Policymakers and funding organizations also have a crucial role. They must support this research and ensure new technologies can be safely and quickly brought to market.

Finally, raising public awareness about neurological disorders is essential. The more people understand these conditions, the better support systems we can create for those affected. This also helps reduce the stigma around neurological disorders, making it easier for people to seek help.

In summary, neuroengineering offers countless opportunities to innovate and improve the lives of those with neurological disorders. By embracing new technologies and working together across disciplines, we can make significant strides in understanding, treating, and preventing these conditions. So, whether you're just starting your studies or already deep into research, now is the time to get involved and make an impact.



# Chapter 12: Learning activities

## Learning Activity 12.1

### *Activity: Identifying Neurological Disorders in Case Studies*



#### ***Objective***

Students will analyze case studies to identify neurological disorders and respond to questions to deepen their understanding of neurocognitive disorders.

#### ***Materials***

- Internet access
- Computers or tablets
- Printed or digital copies of the case study: [Case Studies: Neurocognitive Disorders](#)
- Note-taking materials (paper, pens, or digital tools)

#### ***Time***

30-40 minutes

#### ***Instructions***

##### ***Introduction (5 minutes):***

Introduce the activity and explain its goal: to identify neurological disorders through analyzing case studies.

1. Briefly overview the importance of understanding neurocognitive disorders in neuroengineering and psychology.

##### ***Case Study Analysis (20 minutes):***

3. Distribute printed or digital copies of the case study to each student or group.
4. Instruct students to read the case study carefully and take notes on key symptoms, behaviors, and any relevant background information.

***Question Response (10 minutes):***

5. Ask students to respond individually or in groups to the questions in the case study. Ensure they reference specific details from the case to support their answers.

***Group Discussion (5 minutes):***

6. Facilitate a class discussion where students can share their findings and compare their answers. Encourage them to explain their reasoning and listen to different perspectives.

***Conclusion (5 minutes):***

7. Summarize the key points from the discussion, highlighting the identified neurological disorders and the symptoms that led to these conclusions. 8. Emphasize the relevance of these skills in real-world applications, such as diagnosing and treating neurocognitive disorders.

---

## **Learning Activity 12.2**

### ***Activity: Discovery Challenge - Identifying Neuro Diseases from NIH FOAs***

#### ***Objective***

Students will explore the NIH website to quickly identify and collect a list of neuro diseases mentioned in the published Funding Opportunity Announcements (FOAs).

#### ***Materials***

- Internet access
- Computers or tablets
- Note-taking materials (paper, pens, or digital tools)

#### ***Time***

10 minutes



## ***Instructions***

### ***Introduction (2 minutes):***

1. Introduce the activity and explain its goal: to discover how many neuro diseases are mentioned in the NIH FOAs within a 5-minute time frame.
2. Briefly explain what FOAs are and their relevance in research funding.

### ***Discovery Task (5 minutes):***

3. Instruct students to visit the NIH website and navigate to the section with published FOAs.
4. Ask students to find and list as many neuro diseases as possible within the 5-minute time limit.

### ***Group Sharing (3 minutes):***

5. Have students share the number and names of the neuro diseases they found.
6. Compile a class list on the whiteboard or digital platform, noting any overlaps and unique findings.



## Chapter 12: Lab introduction

In this series of lab exercises, you will explore advanced concepts in neuroscience through practical applications. These labs provide hands-on experience simulating neural activity and neurostimulation, deepening your understanding of how neurological disorders and interventions impact brain function.

In the first lab, you will expand your knowledge of the Hodgkin-Huxley (HH) model by simulating neural activity differences between a healthy brain and a brain affected by Parkinson's disease. You will create a graphical user interface (GUI) to input various parameters and observe their impact on the membrane potential of neurons. This exercise will help you understand how changes in the HH model parameters can represent the effects of neurological diseases.

The second lab combines concepts from neurostimulation, brain-computer interfaces (BCIs), and neurological disorders. You will simulate neurostimulation's impact on conditions like Parkinson's disease and depression using coil designs. Additionally, you will conduct statistical analysis to compare the effects of neurostimulation on these disorders, providing insights into how such interventions can modulate neural activity to alleviate symptoms.



# Chapter 12: Lab Example 1



## *Overview*

In this lab example, we will continue with our Neuron Example in Chapter 2 and focus on modifying parameters for Parkinson's Disease. We will focus on expanding some understanding of the HH model and how diseases in this chapter influence the model.

In this lab example, we will simulate the differences in neural activity between a healthy brain and a brain affected by Parkinson's disease using the Hodgkin-Huxley (HH) model. We will create a graphical user interface (GUI) that allows us to input various parameters and observe their impact on the membrane potential of neurons.

## *Requirements*

1. Python (tested with 3.8 and later)
2. NEURON ([neuron.yale.edu](http://neuron.yale.edu))
3. Matplotlib
4. Tkinter

## **Steps**

The first thing you need to do is go to the GitHub repository for this book. You can find it using this link:

[https://github.com/bddupre92/Neurobook\\_BME\\_UND](https://github.com/bddupre92/Neurobook_BME_UND)

After you have opened the GitHub, you need to navigate to Chapter 12, Lab Example 1. In this lab example, you will find the code for the simulation.

You will want to copy and paste the code into a script named PDNeuronGUI.py.

## *Script Structure*

Define Constants and Parameters:

1. `amp_value`: Amplitude of the current.
2. `duration_value`: Duration of the current.
3. `num_steps_value`: Number of steps in the simulation.

4. dend\_nseg\_value: Number of segments in the dendrite.
5. cm\_value: Membrane capacitance.
6. Ra\_value: Axial resistance.
7. gbar\_hh\_value: Maximum conductance for sodium, potassium, and leak channels.
8. v\_init\_value: Initial membrane potential.

The GUI input will pop-up with pre-populated values for everything. Run the initial example before modifying parameters to assess if this is a good starting point for the HH Model.

### ***Baseline Neural Activity Simulation***

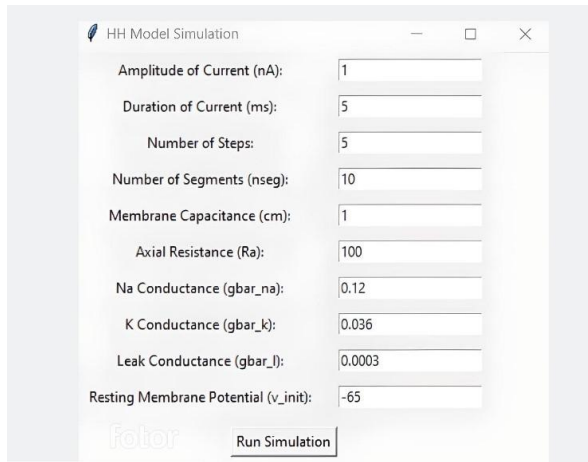
Simulate baseline neural activity with the defined parameters.

### ***Post-Stimulation Neural Activity Simulation***

Simulate neural activity after modifying the parameters to represent Parkinson's disease.

### ***Visualization***

Plot the membrane potential for both the healthy and Parkinson's brain models.



The image shows a software window titled "HH Model Simulation". It contains a list of parameters for a neuron model simulation, each with a corresponding input field. The parameters and their values are:

Parameter	Value
Amplitude of Current (nA):	1
Duration of Current (ms):	5
Number of Steps:	5
Number of Segments (nseg):	10
Membrane Capacitance (cm):	1
Axial Resistance (Ra):	100
Na Conductance (gbar_na):	0.12
K Conductance (gbar_k):	0.036
Leak Conductance (gbar_l):	0.0003
Resting Membrane Potential (v_init):	-65

At the bottom left is the "Fototor" logo, and at the bottom right is a button labeled "Run Simulation".

Figure 12.4: Model Parameters

## ***Explanation of the Figures***

### ***Duration vs. Membrane Potential***

- Fig. 12.5 shows how the duration of the injected current affects the membrane potential.
- By varying the duration, you can observe the impact on the action potential duration and how prolonged stimulation influences the neuron's behavior.

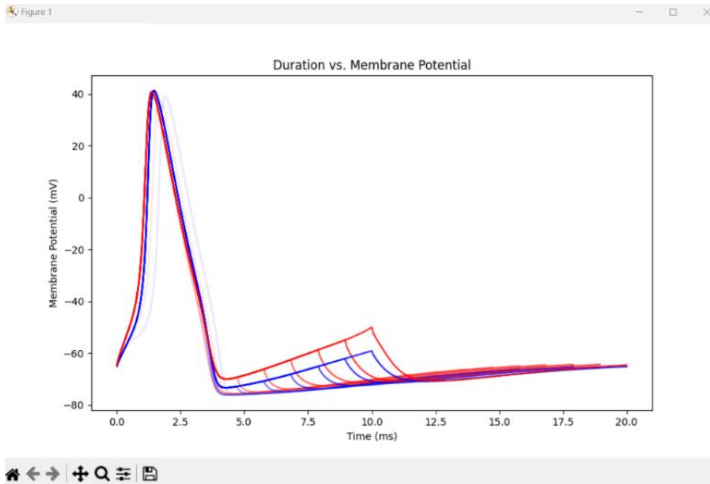


Figure 12.5: Duration vs. Membrane Potential

### ***Current vs. Membrane Potential***

- Fig. 12.6 shows how different amplitudes of the injected current affect the membrane potential for healthy and Parkinson's models.

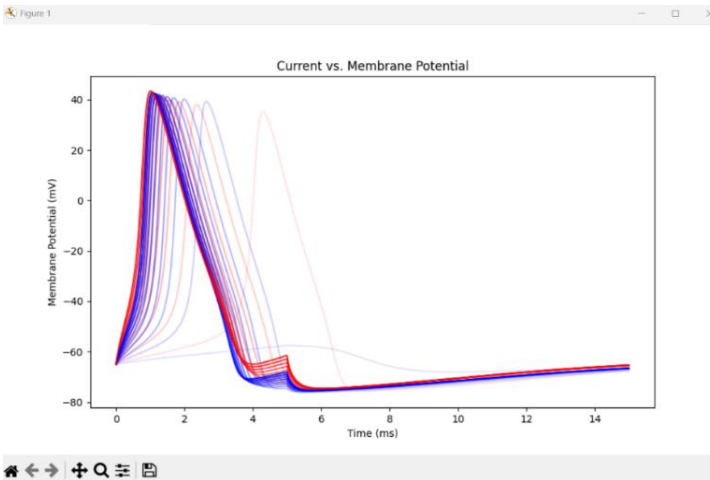


Figure 12.6: Current vs. Membrane Potential

- By varying the current amplitude, you can observe the threshold

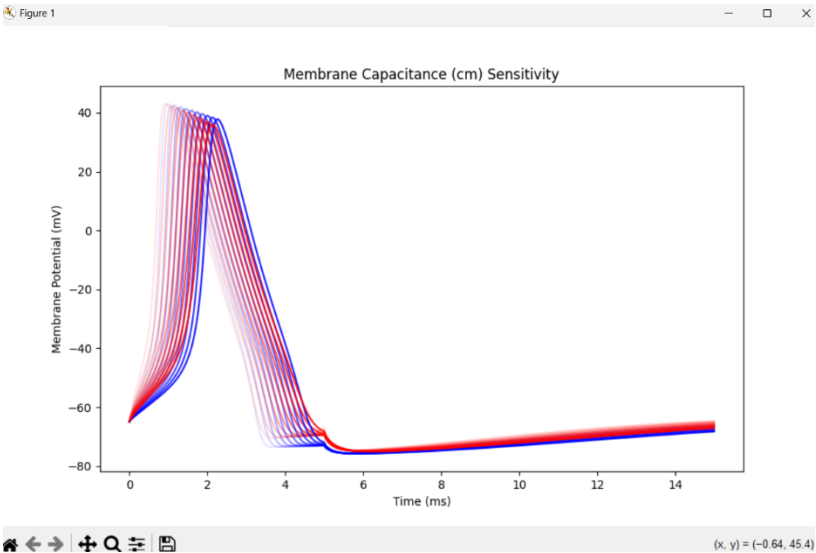


Figure 12.7: Membrane Capacitance (cm) Sensitivity

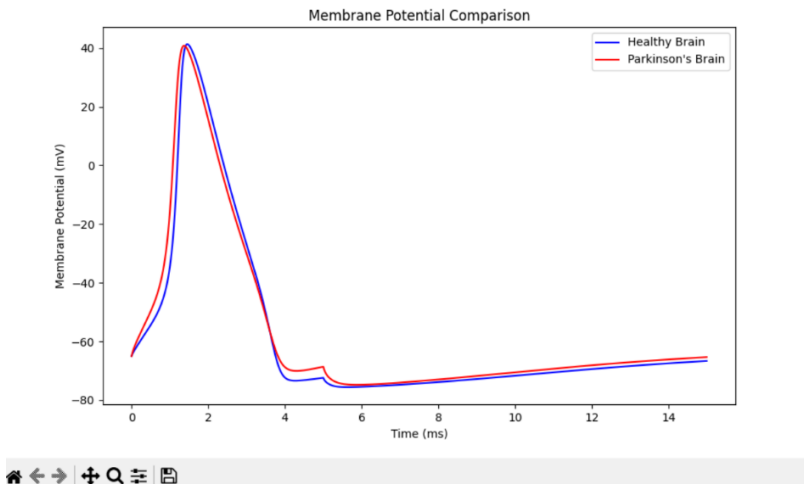


Figure 12.8: Membrane Potential Comparison

behavior and how the neurons respond differently in healthy versus Parkinson's conditions.

## ***Explanation of the Parameter Sensitivity Plots***

### ***Membrane Capacitance ( $C_m$ ) Sensitivity***

- Fig. 12.7 shows how changes in membrane capacitance affect the membrane potential.
- Higher capacitance can make the neuron less responsive, while lower capacitance makes it more responsive.

### ***Axial Resistance ( $R_a$ ) Sensitivity***

- Illustrates the impact of axial resistance on the membrane potential.
- Higher resistance slows down signal propagation, while lower resistance speeds it up.

### ***Sodium Conductance ( $g_{Na}$ ) Sensitivity***

- Displays how changes in sodium conductance influence the action potential.
  - Higher conductance increases excitability, making it easier to trigger action potentials.

### ***Potassium Conductance ( $g_K$ ) Sensitivity***

- Demonstrates the effect of potassium conductance on repolarization.
- Higher conductance leads to quicker repolarization, shortening the action potential duration.

### ***Leak Conductance ( $g_L$ ) Sensitivity***

- Shows how variations in leak conductance affect the membrane potential.
- Higher leak conductance stabilizes the resting membrane potential but reduces overall excitability.

These sensitivity plots help understand the model's robustness and the significance of each parameter in influencing the membrane potential.

## ***Membrane Potential Comparison***

- **Healthy Brain:** The membrane potential Fig. 12.8 for the healthy brain shows the typical action potential characteristics.
- **Parkinson's Brain:** The membrane potential Fig. 12.8 for the Parkinson's brain, modified by changing parameters like dendrite diameter, membrane capacitance, and ion channel conductance, shows how the action potential is affected by Parkinson's disease.

## ***Key Observations***

- The differences in the membrane potential plots illustrate the impact of Parkinson's disease on neural activity.
- The modified parameters in the Parkinson's model result in changes to the amplitude and shape of the action potentials, demonstrating the disease's effect on neuronal excitability.

## ***Suggestions for Parameters to Modify***

To explore the impact of different parameters on action potentials, you can modify the following inputs:

1. Amplitude of Current (nA):
  - Higher amplitudes can increase the likelihood of triggering an action potential.
  - Lower amplitudes might not reach the threshold for an action potential.
2. Duration of Current (ms):
  - Longer durations can sustain depolarization, potentially leading to multiple action potentials.
  - Shorter durations might only cause a brief depolarization without reaching the threshold.
3. Membrane Capacitance (cm):
  - Increasing capacitance makes the membrane less responsive to voltage changes, slowing down action potential initiation.
  - Decreasing capacitance makes the membrane more responsive, speeding up action potential initiation.

4. Axial Resistance ( $R_a$ ):
  - Higher resistance can reduce the speed of signal propagation along the neuron.
  - Lower resistance can increase the speed of signal propagation.
5. Sodium Conductance ( $g_{Na}$ ):
  - Increasing sodium conductance can enhance the neuron's excitability, making it easier to trigger action potentials.
  - Decreasing sodium conductance can reduce excitability.
6. Potassium Conductance ( $g_K$ ):
  - Increasing potassium conductance can lead to quicker repolarization and a shorter action potential duration.
  - Decreasing potassium conductance can prolong repolarization and action potential duration.
7. Leak Conductance ( $g_L$ ):
  - Higher leak conductance can stabilize the resting membrane potential but reduce overall excitability.
  - Lower leak conductance can increase excitability but may make the neuron more prone to spontaneous activity.
  - Resting Membrane Potential ( $V_{init}$ ):
    - A more negative resting potential (hyperpolarized) makes reaching the threshold for an action potential harder.
    - A less negative resting potential (depolarized) makes it easier to reach the threshold.

### ***What the Output Means***

- **Action Potential Amplitude:** Indicates the strength of the neural signal. Changes in amplitude can reflect alterations in ion channel conductance or membrane properties.
- **Action Potential Duration:** Affects the timing and pattern of neural signaling. Prolonged action potentials can indicate issues with ion channel kinetics.

- **Threshold:** The minimum membrane potential required to trigger an action potential. Changes in the threshold can indicate alterations in membrane excitability.
- **Repolarization Phase:** The phase during which the membrane potential returns to the resting state. Alterations in this phase can reflect changes in potassium conductance or other repolarizing mechanisms.

By systematically modifying these parameters, you can gain insights into how different factors contribute to the overall behavior of neurons in both healthy and diseased states. This understanding can help in developing targeted therapies for neurological disorders like Parkinson's disease.



# Chapter 12: Lab Example 2



## Overview

In this lab example, we will combine some concepts you have learned from the textbook: neurostimulation (Chapter 7), BCIs (Chapter 6), and disorders (Chapter 12). As you have learned, neurostimulation can modulate neural activity to alleviate symptoms of conditions such as Parkinson's disease, chronic pain, epilepsy, and depression. For instance, deep brain stimulation (DBS) is a widely used form of neurostimulation that targets brain regions to reduce tremors and improve motor function in Parkinson's patients. Similarly, spinal cord stimulation (SCS) is employed to manage chronic pain by altering pain signal transmission in the spinal cord. In this lab example, we will use the coil design from Chapter 6: Lab Example to simulate neurostimulation between simulated Parkinson's Disease and Depression. Then, we will do some statistical analysis (like the one in Chapter 5: Lab Example 2) to see how neurostimulation impacts these disorders differently.

## Requirements

MATLAB (tested with R2021a and later)

## Steps

The first thing you need to do is go to the GitHub repository for this book. You can find it using this link:

[https://github.com/bddupre92/Neurobook\\_BME\\_UND](https://github.com/bddupre92/Neurobook_BME_UND)

After you have opened the GitHub, you need to navigate to Chapter 12 Lab Example 2. In this lab example, you will find three scripts.

- *Rtmscoildepression.m*
- *Rtmscoilforjustparkinsons.m*
- *Ttestrtmscoil.m*

You will want to copy and paste each code into its separate script.

We will run the RTMS Coil for Parkinson's and then the RTMS Coil for Depression. The scripts follow the following structure.

## ***Script Structure***

### ***Define Constants and Parameters***

mu0: Permeability of free space.

num\_points: Number of points in each dimension for the grid.

coil\_radius, coil\_center, frequencies, currents, phases: Parameters defining the neurostimulation coils.

### ***Observation Grid***

Define a 3D grid to simulate the brain model.

Baseline Neural Activity Simulation:

Simulate baseline neural activity with altered oscillatory patterns for depression.

### ***Magnetic Stimulation***

Calculate the magnetic field produced by the neurostimulation coils.

Post-Stimulation Neural Activity Simulation:

Simulate neural activity after magnetic stimulation.

Time-Varying MEG Signal Calculation:

Calculate the MEG signal over time.

### ***Visualization***

Plot the magnetic field slices before and after stimulation.

Plot the MEG signal over time.

## ***Major Functions Used in the Script***

### ***meshgrid***

- **Usage:** `[x, y, z] = meshgrid(linspace(-0.1, 0.1, num_points), linspace(-0.1, 0.1, num_points), linspace(-0.1, 0.1, num_points));`
- **Purpose:** Creates a 3D grid of points representing the observation space for the brain model.

### ***space***

- **Usage:** `linspace(-0.1, 0.1, num_points)`
- **Purpose:** Generates linearly spaced vectors for defining the grid points in the x, y, and z dimensions.

### *sin*

- **Usage:** `sin(2 * pi * f_beta * t(i))`
- **Purpose:** Calculates the sine of an angle, which is used here to simulate oscillatory patterns in the MEG signals.

### *subplot*

- **Usage:** `subplot(2, 2, 1);`
- **Purpose:** Creates a subplot in a figure for plotting multiple graphs in a single window.

### *imagesc*

- **Usage:** `imagesc(linspace(-0.1, 0.1, num_points), linspace(-0.1, 0.1, num_points), meg_baseline_slice);`
- **Purpose:** Displays a scaled color image of the 2D matrix to visualize the magnetic field slices.

### *squeeze*

- **Usage:** `meg_baseline_slice = squeeze(meg_baseline(:, :, slice_index));`
- **Purpose:** Removes singleton dimensions from an array used here to extract a 2D slice from the 3D magnetic field data.

### *plot*

- **Usage:** `plot(t, meg_baseline_time(:, slice_index), 'DisplayName', 'Baseline');`
- **Purpose:** Plot data points in 2D space, which are used here to visualize the MEG signals over time.

### *hold on / hold off*

- **Usage:** `hold on;` and `hold off;`
- **Purpose:** Retains the current plot and certain settings so that subsequent graphing commands add to the existing graph.

### *legend*

- **Usage:** `legend;`
- **Purpose:** Adds a legend to the plot to label different data series.

### *title*

- **Usage:** `title('Baseline Magnetic Field (z=0)');`
- **Purpose:** Adds a title to the plot.

### *xlabel / ylabel*

- **Usage:** xlabel('x (m)'); and ylabel('y (m)');
- **Purpose:** Add labels to the plot on the x-axis and y-axis.

### *colorbar*

- **Usage:** colorbar;
- **Purpose:** Adds a color bar to the plot to indicate the color scale.

### *clim*

- **Usage:** clim([cmin cmax]);
- **Purpose:** Set the plot's color limits to ensure consistent color scaling across different plots.

When you run the functions, you will generate two figures. One for Parkinson's Disease will look like Fig. 12.9, and one for depression will look like Fig. 12.10.

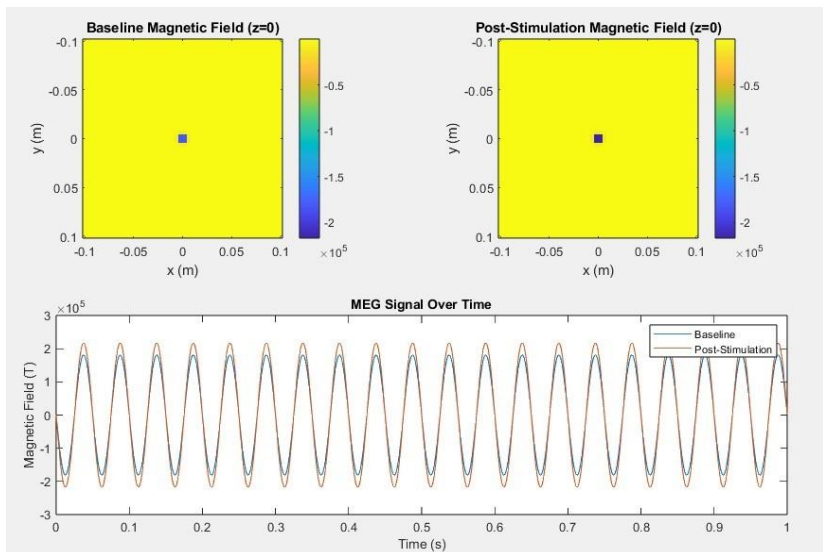


Figure 12.9: MEG Signal Over Time for Parkinson's Disease

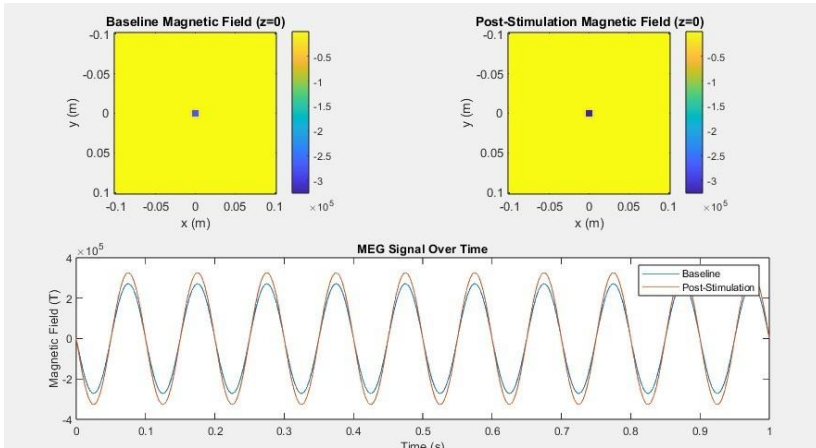


Figure 12.10: MEG Signal Over Time for Depression

## ***Explanation of the Figures***

These figures demonstrate the simulation results of neurostimulation effects on MEG signals in a simplified brain model. Here are explanations of each plot of the statistics.

### ***Top Row: Magnetic Field Slices***

#### ***Left Plot: Baseline Magnetic Field ( $z=0$ )***

- This plot shows the baseline magnetic field slice at the middle plane of the brain model ( $z=0$ ) before any stimulation is applied.
- The color bar indicates the strength of the magnetic field in Tesla (T), with blue regions representing negative field values and yellow regions representing positive field values.

#### ***Right Plot: Post-Stimulation Magnetic Field ( $z=0$ )***

- This plot shows the magnetic field slice at the middle plane of the brain model ( $z=0$ ) after the neurostimulation has been applied.
- The color bar again indicates the strength of the magnetic field in Tesla (T).
- The difference between the baseline and post-stimulation plots demonstrates the effect of neurostimulation on the magnetic field.

## ***Bottom Row: MEG Signal Over Time***

### ***Plot: MEG Signal Over Time***

- This plot shows the MEG signal at the brain model's central point (slice) over time (1 second).
- The x-axis represents time in seconds (s), and the y-axis represents the magnetic field in Tesla (T).
- Two lines are plotted:
  - **Blue Line (Baseline):** Represents the MEG signal before stimulation.
  - **Orange Line (Post-Stimulation):** Represents the MEG signal after stimulation.
- The differences in amplitude and phase between the baseline and post-stimulation signals indicate how neurostimulation affects neural oscillations and activity.

### ***Key Observations***

- **Magnetic Field Slices:** The baseline and post-stimulation magnetic field slices show how the applied stimulation alters the magnetic field distribution within the brain model.
- **MEG Signal Over Time:** The post-stimulation MEG signal exhibits slight changes in amplitude and phase compared to the baseline, illustrating the impact of neurostimulation on neural activity. These changes can be indicative of altered neural oscillatory patterns due to stimulation.

## **Statistical Analysis**

Both figures look similar, and it is hard to understand if there are any differences. This is why it is important to understand statistical analysis techniques and how to use them in MATLAB. In this example, Please refer to Chapter 5: Lab Example 2 for a detailed explanation of a t-test. Go back to the final code in MATLAB called t-test rtms coil and click run.

# Script Structure

## *Perform t-test*

Use `ttest2` to compare the difference in MEG signal changes between depression and Parkinson's disease.

## *Display Results*

Print the p-value, t-statistic, degrees of freedom, and conclusion about the null hypothesis based on the t-test results.

## *Major Functions Used in the Script*

### *ttest2*

- **Usage:** `[~, p_value_diff, ~, stats_diff] = ttest2(meg_post(:) - meg_baseline_alpha(:), meg_post_beta(:) - meg_baseline_beta(:));`
- **Purpose:** Performs a two-sample t-test to compare the means of two independent samples. This script is used to compare the differences in MEG signals before and after stimulation between depression and Parkinson's disease conditions.
- **Outputs:**
  - `p_value_diff`: The p-value of the t-test.
  - `stats_diff`: A structure containing the t-statistic, degrees of freedom, and other relevant information.

### *disp*

- **Usage:** `disp(['P-value for t-test for the difference between Depression and Parkinson"s: ', num2str(p_value_diff)]);`
- **Purpose:** Displays text or variables in the Command Window. It is used here to print the p-value, t-statistic, degrees of freedom, and conclusion about the null hypothesis.

### *num2str*

- **Usage:** `num2str(p_value_diff)`
- **Purpose:** Converts numbers to a string format. This is useful for concatenating numerical values with text for display purposes.

Once you have run this code, you will get some results in your Command Window.

### ***Explanation of the Results***

The statistical analysis performed using a two-sample t-test compares the differences in the effects of neurostimulation between depression and Parkinson's disease. The results of the t-test are as follows:

#### ***P-value: 0.012806***

The p-value measures the probability that the observed differences between the two conditions could have occurred by random chance. A p-value less than 0.05 is typically considered statistically significant.

In this case, the p-value is 0.012806, less than 0.05. This indicates that the differences in the effects of neurostimulation between depression and Parkinson's disease are statistically significant.

#### ***t-statistic: -2.4891***

The t-statistic measures the size of the difference relative to the variation in the sample data. A larger absolute value of the t-statistic indicates a more significant difference between the groups.

Here, the t-statistic is -2.4891, which suggests a noticeable difference between the two conditions.

#### ***Degrees of Freedom: 249998***

Degrees of freedom (df) refers to the number of independent values that can vary in the analysis. In the context of a t-test, it is used to determine the distribution of the test statistic.

The degrees of freedom for this test are 249998, which is typical for a large dataset.

## ***Results Conclusion***

We reject the null hypothesis based on the p-value being less than 0.05. The null hypothesis states that there is no significant difference in the effects of neurostimulation between depression and Parkinson's disease.

The results indicate that there is a significant difference in how neurostimulation affects individuals with depression compared to those with Parkinson's disease.

## **Summary**

In this lab example, we explored the effects of neurostimulation on neural activity for two neurological conditions: Parkinson's disease and depression. Using MATLAB scripts, we simulated the magnetic fields and MEG signals before and after neurostimulation for both conditions and then performed a statistical analysis to compare the differences in effects.

### ***The key findings from this lab include:***

#### ***Simulation Results***

The magnetic field distribution and MEG signals were visualized for baseline and post-stimulation conditions.

Differences in amplitude and phase between baseline and post-stimulation MEG signals were observed, indicating the impact of neurostimulation on neural activity.

#### ***Statistical Analysis***

A two-sample t-test was performed to statistically compare the effects of neurostimulation between depression and Parkinson's disease.

The p-value obtained (0.012806) was less than the significance threshold of 0.05, indicating a statistically significant difference in the effects of neurostimulation between the two conditions.

The t-statistic (-2.4891) further confirmed the noticeable difference, and the degrees of freedom (249998) highlighted the robustness of the analysis due to the large dataset.

### ***Interpretation***

The results indicate that neurostimulation affects individuals with depression differently compared to those with Parkinson's disease. This underscores the importance of tailoring neurostimulation treatments to specific neurological conditions to achieve the best therapeutic outcomes.

This lab example combines concepts from neurostimulation, brain-computer interfaces (BCIs), and neurological disorders to comprehensively understand how neurostimulation can modulate neural activity differently across various conditions. The statistical analysis demonstrates the importance of using quantitative methods to validate the efficacy and specificity of neurostimulation treatments, highlighting the potential for personalized therapeutic approaches in clinical practice.

Overall, this lab example practically applies theoretical knowledge, reinforcing the significance of interdisciplinary approaches in biomedical engineering and neuroscience.



# General Conclusion

This book, "Introduction to Neuroengineering," has aimed to provide a comprehensive overview of the principles and applications within this interdisciplinary field. The convergence of neuroscience, engineering, and technology represents a frontier with potential for innovation in medical devices, neural interfaces, and therapeutic strategies. By offering this resource as an Open Educational Resource (OER), we hope to foster a collaborative and accessible learning environment for students, educators, and professionals. The journey through this book reflects the collective efforts and dedication of numerous individuals whose contributions have been invaluable.

Neuroengineering, as explored throughout this book, stands at the intersection of multiple disciplines, drawing on advances in neural science, electrical engineering, computer science, and biomedical engineering. This approach allows for novel solutions to complex problems related to the human nervous system. From neural prosthetics that restore lost functions to brain-computer interfaces that open new avenues for communication and control, the innovations within neuroengineering are geared to revolutionize both healthcare and our understanding of the human brain.

One of the key themes cultivated in this book is the importance of interdisciplinary collaboration. The field of neuroengineering thrives on the integration of diverse perspectives and expertise. By bringing together neuroscientists, engineers, clinicians, and computer scientists, we can tackle challenges that no single discipline could address alone. This collaborative spirit is essential for advancing research and translating discoveries into practical applications that can benefit society.

As we conclude this journey through the foundational concepts and cutting-edge advancements in neuroengineering, it is important to reflect on our work's ethical considerations and societal implications. The technologies and techniques developed in this field have the potential to impact human lives profoundly. Therefore, we must approach our research and development efforts with a strong ethical framework, ensuring that the benefits of neuroengineering are accessible to all and the potential risks are carefully

managed. Ethical considerations, such as privacy, consent, and the long-term effects of neural interventions, must remain at the forefront of our discussions and decisions.

Education and outreach also play a pivotal role in the future of neuroengineering. By making this book available as an OER, we aim to democratize and decolonize access to knowledge and inspire the next generation of neuroengineers. We hope students and educators from diverse backgrounds will use this resource to gain a solid foundation in the field and contribute their unique perspectives and ideas. The future of neuroengineering depends on the continuous influx of fresh, innovative minds eager to push the boundaries of what is possible.

Furthermore, the practical applications of neuroengineering are great and varied. This book has explored several key areas, including neural prosthetics, brain-machine interfaces, neural imaging, and neuromodulation. Each area holds promise for significant advancements in medical treatment and quality of life. For example, neural prosthetics can potentially restore mobility and independence to individuals with limb loss, while brain-machine interfaces could provide new communication channels for those with severe motor impairments. Advances in neural imaging can lead to better diagnostic tools, and a deeper understanding of brain disorders, and neuromodulation techniques offer new avenues for treating conditions such as epilepsy and depression.

The journey of creating this book has been a testament to the power of collaboration and the collective pursuit of knowledge. The support and contributions from various individuals and institutions have been instrumental in bringing this project to fruition. As we move forward, it is essential to continue fostering an environment of collaboration, innovation, and ethical responsibility. The challenges we face in neuroengineering are complex, but they are also opportunities to make a meaningful impact on human health and well-being.

In summary, "Introduction to Neuroengineering" is more than just a textbook; it is a stepping stone toward a future where the boundaries between biology and technology are seamlessly integrated for the betterment of humanity. We hope this resource will inspire, educate, and empower readers to contribute to the exciting and ever-evolving field of neuroengineering. The journey does not end here; it is only the beginning. As discoveries are made and technologies are developed, the principles and ideas discussed in this book will continue to evolve, driving the field forward and opening up new possibilities for understanding and enhancing the human experience.



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**Terry, Tubbs, Dupre, Fugger, Alvarez**

"The human brain is the last, and greatest, scientific frontier" –James D. Watson

"Introduction to Neuroengineering" serves as a comprehensive guide to the fast-evolving field at the intersection of neuroscience, engineering, and technology. This book covers foundational concepts like neuron structure, action potentials, and neural modeling, moving through advanced topics like brain-computer interfaces (BCIs), neurostimulation, and imaging technologies (EEG, MEG, fMRI). Each chapter combines theory with practical exercises and lab examples, accessible through a GitHub repository to enhance hands-on learning. Aimed at students, educators, and professionals, this resource offers a foundation and inspiration for innovation in neuroengineering, promoting ongoing exploration in this impactful field.

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# **INTRODUCTION TO NEUROENGINEERING**

